

⁶⁴⁵ **Supplementary Figures and Tables**

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
3	IGF2BP2	C3orf65,IGF2BP2	Thyroid	7.5	8.6e-14	5.9	4.8e-09	8.8	1.1e-18
4	WFS1	WFS1,PPP2R2C	Brain-Cerebellum	5.2	1.6e-07	3.9	0.00011	6.2	5.7e-10
4	WFS1	WFS1,PPP2R2C	Nerve-Tibial	5.5	3.7e-08	4.5	6.5e-06	6.4	1.7e-10
4	WFS1	WFS1,PPP2R2C	Skin-Not-Sun-Exposed-Suprapubic	5.3	1.4e-07	5	5.5e-07	6.6	4.6e-11
4	WFS1	WFS1,PPP2R2C	Skin-Sun-Exposed-Lower-leg	5.7	1.1e-08	4.6	4.7e-06	6.6	4.3e-11
4	WFS1	WFS1,PPP2R2C	Thyroid	5.4	7.8e-08	4.7	2.1e-06	6.6	3.5e-11
6	ID4	CDKAL1	Vagina	-6.2	6.3e-10	-4.7	2.4e-06	-7.9	2.1e-15
6	HLA-A	none reported	Skin-Sun-Exposed-Lower-leg	5.4	5.1e-08	0.68	0.5	4.5	7.5e-06
7	JAZF1	JAZF1	Adipose-Subcutaneous	-7	3.3e-12	-6.8	9.8e-12	-8.5	2.4e-17
7	JAZF1	JAZF1	Adipose-Visceral-Omentum	-8.1	3.7e-16	-5.8	5.5e-09	-9.5	3.1e-21
7	JAZF1	JAZF1	Artery-Aorta	-5.9	4.7e-09	-4.7	2e-06	-6.8	7.5e-12
7	JAZF1	JAZF1	Artery-Tibial	-7.2	4.8e-13	-6.8	1.5e-11	-9	2e-19
7	JAZF1	JAZF1	Cells-Transformed-fibroblasts	-7	3.1e-12	-3.9	0.00012	-7.2	6.5e-13
7	JAZF1	JAZF1	Muscle-Skeletal	-8.5	2.5e-17	-5.6	2.4e-08	-9.4	5.9e-21
7	JAZF1	JAZF1	Pancreas	-7	1.8e-12	-5.5	3.2e-08	-8.3	1.3e-16
8	CCNE2	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Whole-Blood-DGN	-5.5	9e-08	-1	0.31	-4.7	3e-06
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Skin-Sun-Exposed-Lower-leg	-5.3	1.2e-07	-0.43	0.66	-4.2	2.2e-05
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Testis	-5.4	6.9e-08	-0.57	0.57	-4.6	5.1e-06
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Whole-Blood-DGN	5.2	1.9e-07	0.98	0.33	4.4	1.1e-05
9	CDKN2A	CDKN2B,DMRTA1	Adrenal-Gland	-5.7	1.1e-08	-3	0.003	-6.2	4.5e-10
9	ANKRD20A1	none reported	Breast-Mammary-Tissue	5.5	4.4e-08	0.92	0.36	4.8	1.9e-06
10	CAMK1D	CDC123,CAMK1D	Whole-Blood	6	2.4e-09	3.4	0.00066	6.3	2.9e-10
10	CAMK1D	CDC123,CAMK1D	Whole-Blood-DGN	5.3	8.9e-08	3.7	0.00018	5.9	4.7e-09
10	NUDT5	CDC123,CAMK1D	Whole-Blood-DGN	5.7	1.1e-08	3.5	0.00049	6	2e-09
10	HHEX	IDE,KIF11,HHEX	Cells-Transformed-fibroblasts	-6.9	5.9e-12	-3.8	0.00013	-7.1	1.2e-12
10	HHEX	IDE,KIF11,HHEX	Whole-Blood-DGN	-6.3	3.2e-10	-2.8	0.0046	-6.1	9.3e-10
10	CYP28C1	IDE,KIF11,HHEX	Adipose-Subcutaneous	-6.4	1.5e-10	-2.8	0.0053	-6.1	9.3e-10
10	CWF19L1	none reported	Breast-Mammary-Tissue	-5.5	4.6e-08	-0.76	0.45	-4.7	2.9e-06
10	TCF7L2	TCF7L2	Artery-Aorta	-9.5	2.5e-21	-8.9	8.7e-19	-12	2e-31
10	DCLRE1A	TCF7L2	Cells-Transformed-fibroblasts	5.9	3.3e-09	5.2	2e-07	7	1.8e-12
10	DCLRE1A	TCF7L2	Thyroid	-7.4	1.1e-13	-5	4.7e-07	-8.4	4.9e-17
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Breast-Mammary-Tissue	-5.7	1.5e-08	-3.9	8.4e-05	-6.4	1.3e-10
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Esophagus-Mucosa	-5.4	8.4e-08	-2.8	0.0044	-5.6	2.7e-08
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Nerve-Tibial	-5.6	2.6e-08	-3.3	0.00092	-5.8	5e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Small-Intestine-Terminal-Ileum	5.2	1.9e-07	3.5	0.00046	6.3	2.2e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Artery-Aorta	5.4	6e-08	3.1	0.0022	5.7	1.4e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Artery-Tibial	5.3	1.5e-07	3.4	0.00077	5.8	7.8e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Cortex	5.7	1.4e-08	3.1	0.0018	6.2	5.7e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Frontal-Cortex-BA9	5.7	1.5e-08	3	0.0031	6.3	2.7e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Breast-Mammary-Tissue	5.2	1.6e-07	2.7	0.0079	5.5	4.9e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Colon-Sigmoid	5.5	4.9e-08	2.6	0.0097	5.7	1.3e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Colon-Transverse	5.5	4.9e-08	3.2	0.0013	5.8	5.5e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Esophagus-Gastroesophageal-Junction	5.4	5.1e-08	2.4	0.015	5.7	1.4e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Nerve-Tibial	5.5	3e-08	3.2	0.0014	5.8	7.9e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Skin-Not-Sun-Exposed-Suprapubic	5.2	1.8e-07	3	0.0027	5.6	2.8e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Skin-Sun-Exposed-Lower-leg	5.2	2.2e-07	3.1	0.0019	5.5	4.5e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Stomach	5.7	1.4e-08	3.2	0.0012	6.2	6.1e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Testis	5.2	2.1e-07	3.2	0.0015	5.7	1e-08
15	HMG20A	PEAK1,HMG20A,LINGO1	Pituitary	5.5	4.5e-08	3.4	0.00065	6.2	6.7e-10

Table S1. Bonferroni significant T2D associated genes from the trans-ethnic MetaXcan study. Results for genes and corresponding models that meet Bonferroni significance in the trans-ethnic analysis are shown with nearby genes and results from the GERA replication study and meta-analysis of the trans-ethnic and GERA Metaxcan associations. 20 genes pass the stringent Bonferroni correction. Blue shading denotes putative novel T2D genes that are not the most proximal to GWAS associations at $p < 5 \times 10^{-6}$. Replication in the GERA study at $FDR_{rep} < 0.05$ is denoted by a pink outline. Pink and red shading denote Bonferroni significance in at least one model and across all models, respectively, for results from meta-analysis of MetaXcan results.

Attached file t2d-discovery-FDR-0.05.csv

Table S2. Significant associations between predicted expression and T2D.

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
1	<i>CEP85</i>	none reported	Brain–Anterior–cingulate–cortex–BA24	-4.2	2.2e-05	-1.4	0.17	-4.3	2e-05
1	<i>UBIAD1</i>	none reported	Breast–Mammary–Tissue	4.1	4.1e-05	-0.19	0.85	3.1	0.0018
1	<i>CD101</i>	none reported	Whole–Blood–DGN	4.1	3.6e-05	1.6	0.1	3.9	9.3e-05
2	<i>RIF1</i>	none reported	Brain–Frontal–Cortex–BA9	-4.7	2.7e-06	-0.8	0.42	-4.3	1.4e-05
2	<i>MEIS1</i>	none reported	Cells–Transformed–fibroblasts	4.1	3.7e-05	-0.28	0.78	3	0.0027
2	<i>MEIS1</i>	none reported	Testis	4.2	2.9e-05	1.2	0.24	3.9	9.4e-05
2	<i>NRBP1</i>	none reported	Nerve–Tibial	-4.1	3.8e-05	-1.4	0.17	-3.8	0.0014
2	<i>ETAA1</i>	none reported	Thyroid	-4.2	2.8e-05	-0.8	0.43	-3.7	0.00022
2	<i>THADA</i>	<i>THADA</i>	Adipose–Subcutaneous	4.2	2.7e-05	3	0.0024	4.6	4.4e-06
3	<i>IGF2BP2</i>	<i>C3orf65,IGF2BP2</i>	Thyroid	7.5	8.6e-14	5.9	4.8e-09	8.8	1.1e-18
3	<i>SENP2</i>	<i>C3orf65,IGF2BP2</i>	Adrenal–Gland	5.1	3.7e-07	0.5	0.62	4.4	1e-05
3	<i>SFMBT1</i>	none reported	Breast–Mammary–Tissue	4.1	3.6e-05	1.5	0.13	4	6.2e-05
3	<i>POC1A</i>	none reported	Liver	-4.1	4.6e-05	-0.55	0.58	-3.5	0.00055
3	<i>RPP14</i>	none reported	Skin–Sun–Exposed–Lower–leg	-4.1	3.8e-05	-0.92	0.36	-3.6	0.00034
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Brain–Cerebellar–Hemisphere	4.6	5e-06	4	6.4e-05	5.8	5.3e-09
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Brain–Cerebellum	5.2	1.6e-07	3.9	0.00011	6.2	5.7e-10
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Cells–Transformed–fibroblasts	4.4	1.3e-05	3.2	0.0015	4.9	1.1e-06
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Heart–Left–Ventricle	4.2	2.3e-05	2.7	0.0066	4.7	3e-06
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Nerve–Tibial	5.5	3.7e-08	4.5	6.5e-06	6.4	1.7e-10
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Skin–Not–Sun–Exposed–Suprapubic	5.3	1.4e-07	5	5.5e-07	6.6	4.6e-11
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Skin–Sun–Exposed–Lower–leg	5.7	1.1e-08	4.6	4.7e-06	6.6	4.3e-11
4	<i>WFS1</i>	<i>WFS1,PPP2R2C</i>	Thyroid	5.4	7.8e-08	4.7	2.1e-06	6.6	3.5e-11
4	<i>EVC</i>	<i>WFS1,PPP2R2C</i>	Spleen	5.1	4.1e-07	3.7	0.00022	6.2	5.1e-10
5	<i>MAST4</i>	none reported	Muscle–Skeletal	-4.5	5.8e-06	-0.25	0.8	-3.7	0.00026
5	<i>TXNDC15</i>	<i>TXNDC15,PCBD2</i>	Adipose–Subcutaneous	5	4.9e-07	1.3	0.18	4.4	1.1e-05
5	<i>TXNDC15</i>	<i>TXNDC15,PCBD2</i>	Artery–Tibial	4.4	1.3e-05	1.7	0.088	4.2	2.1e-05
5	<i>TXNDC15</i>	<i>TXNDC15,PCBD2</i>	Esophagus–Mucosa	4.4	1.2e-05	2.6	0.0081	4.7	2.5e-06
5	<i>PCBD2</i>	<i>TXNDC15,PCBD2</i>	Whole–Blood–DGN	-4.6	5.1e-06	-1.7	0.081	-4.3	1.8e-05
5	<i>SAR1B</i>	<i>TXNDC15,PCBD2</i>	Liver	4.1	3.5e-05	0.089	0.93	3.3	0.0011
6	<i>TRIM39</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Whole–Blood	5.1	3.7e-07	1.2	0.22	4.5	5.9e-06
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Lung	4.1	3.8e-05	1.4	0.15	3.8	0.00012
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Adipose–Subcutaneous	4.3	1.5e-05	1.2	0.24	3.8	0.00015
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Artery–Tibial	4.2	3.3e-05	1.3	0.2	3.9	1e-04
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Colon–Sigmoid	4.2	3.1e-05	1.2	0.23	3.9	7.9e-05
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Liver	4.1	4.7e-05	1.7	0.083	4	5.2e-05
6	<i>HCG27</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Spleen	4.7	2.6e-06	1.3	0.2	4.6	3.9e-06
6	<i>C2</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Adipose–Subcutaneous	4.3	1.5e-05	3.5	0.00049	4.9	9.5e-07
6	<i>CYP21A2</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Adipose–Visceral–Omentum	4.1	4.5e-05	2	0.046	4.3	2e-05
6	<i>DHX16</i>	<i>CCHCR1,TCF19,POU5F1,HCG27</i>	Brain–Cerebellar–Hemisphere	4.2	3e-05	1.7	0.085	4.3	1.6e-05
6	<i>ID4</i>	<i>CDKAL1</i>	Vagina	-6.2	6.3e-10	-4.7	2.4e-06	-7.9	2.1e-15

Table S3. Tissue-level predicted gene expression associations meet genome-wide significance ($FDR \leq 0.05$) in cross-tissue MetaXcan analysis of the trans-ethnic study.

Results for genes and corresponding models that meet Bonferroni significance in the trans-ethnic analysis are shown with nearby genes and results from the GERA replication study and meta-analysis of trans-ethnic and GERA Metaxcan associations. Blue shading denotes putative novel T2D genes that are not the most proximal to GWAS associations at $p < 5 \times 10^{-6}$. Replication in the GERA study at $p < 0.05$ is denoted by a pink outline. Pink and red shading denote Bonferroni significance in at least one model and across all models, respectively, for results from meta-analysis of MetaXcan results.

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
6	FAM229B	none reported	Skin-Sun-Exposed-Suprapubic	-4.1	4e-05	0.89	0.37	-2.7	0.0061
6	KCNK17	none reported	Esophagus-Mucosa	-4.4	8.6e-06	-2.1	0.04	-4.5	8e-06
6	HLA-A	HLA-A	Skin-Sun-Exposed-Lower-leg	5.4	5.1e-08	0.68	0.5	4.5	7.5e-06
7	ETV1	ETV1,DGKB	Cells-Transformed-fibroblasts	-5.1	3.3e-07	-1.1	0.27	-4.4	9.7e-06
7	JAZF1	JAZF1	Adipose-Subcutaneous	-7	3.3e-12	-6.8	9.8e-12	-8.5	2.4e-17
7	JAZF1	JAZF1	Adipose-Visceral-Omentum	-8.1	3.7e-16	-5.8	5.5e-09	-9.5	3.1e-21
7	JAZF1	JAZF1	Artery-Aorta	-5.9	4.7e-09	-4.7	2e-06	-6.8	7.5e-12
7	JAZF1	JAZF1	Artery-Tibial	-7.2	4.8e-13	-6.8	1.5e-11	-9	2e-19
7	JAZF1	JAZF1	Cells-Transformed-fibroblasts	-7	3.1e-12	-3.9	0.00012	-7.2	6.5e-13
7	JAZF1	JAZF1	Muscle-Skeletal	-8.5	2.5e-17	-5.6	2.4e-08	-9.4	5.9e-21
7	JAZF1	JAZF1	Pancreas	-7	1.8e-12	-5.5	3.2e-08	-8.3	1.3e-16
7	HOXA11	JAZF1	Colon-Sigmoid	4.8	2e-06	3.2	0.0016	5.4	6e-08
7	MRPS33	none reported	Cells-Transformed-fibroblasts	-4.3	2.1e-05	0.22	0.83	-3.1	0.0018
7	MRPS33	none reported	Heart-Atrial-Appendage	-4.3	2.1e-05	0.35	0.73	-3.1	0.0017
8	VDAC3	ANK1	Adrenal-Gland	-4.8	2e-06	-1.3	0.18	-4.6	4.4e-06
8	NDUFAF6	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Cells-Transformed-fibroblasts	-4.5	6e-06	-1.2	0.22	-4	5.2e-05
8	CCNE2	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Cells-EBV-transformed-lymphocytes	4.1	5e-05	0.69	0.49	3.5	0.00043
8	INTS8	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Artery-Tibial	-4.8	1.8e-06	-1.6	0.11	-4.5	6.1e-06
8	INTS8	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Whole-Blood-DGN	-5	4.8e-07	-1.1	0.27	-4.3	1.5e-05
8	CCNE2	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Lung	-4.6	4.2e-06	-0.77	0.44	-3.9	1e-04
8	CCNE2	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Testis	4.5	8e-06	0.61	0.54	3.8	0.00012
8	CCNE2	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Whole-Blood-DGN	-5.5	3e-08	-1	0.31	-4.7	3e-06
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Skin-Sun-Exposed-Lower-leg	-5.3	1.2e-07	-0.43	0.66	-4.2	2.2e-05
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Testis	-5.4	6.9e-08	-0.57	0.57	-4.6	5.1e-06
8	TP53INP1	DPY19L4,INTS8,CCNE2,TP53INP1,NDUFAF6	Whole-Blood-DGN	5.2	1.9e-07	0.98	0.33	4.4	1.1e-05
8	ZNF703	none reported	Adipose-Subcutaneous	-4.1	4.5e-05	-2.3	0.02	-4.2	3.1e-05
8	ZNF34	none reported	Whole-Blood-DGN	4.4	9.5e-06	1.5	0.12	4.1	4.3e-05
8	EXT1	SLC30A8	Brain-Caudate-basal-ganglia	-4.5	6.5e-06	-2.6	0.01	-5.1	3.4e-07
8	MED30	SLC30A8	Brain-Hippocampus	4.6	4.5e-06	0.82	0.41	4.3	1.5e-05
8	RAD21	SLC30A8	Vagina	-4.3	2e-05	-1.7	0.091	-4.6	4e-06
9	CDKN2A	CDKN2B,DMRTA1	Adrenal-Gland	-5.7	1.1e-08	-3	0.003	-6.2	4.5e-10
9	ANKRD20A1	none reported	Breast-Mammary-Tissue	5.5	4.4e-08	0.92	0.36	4.8	1.9e-06
10	HKDC1	C10orf35,RP11-242G20.1	Artery-Aorta	-4.4	9.3e-06	-2.3	0.024	-4.5	6e-06
10	CAMK1D	CDC123,CAMK1D	Heart-Atrial-Appendage	5	6.2e-07	2.5	0.014	5.1	2.9e-07
10	CAMK1D	CDC123,CAMK1D	Heart-Left-Ventricle	4.4	9.3e-06	3.3	0.00081	5.1	2.7e-07
10	CAMK1D	CDC123,CAMK1D	Lung	4.4	1e-05	0.34	0.74	3.5	0.00042
10	CAMK1D	CDC123,CAMK1D	Whole-Blood	6	2.4e-09	3.4	0.00066	6.3	2.9e-10
10	CAMK1D	CDC123,CAMK1D	Whole-Blood-DGN	5.3	8.9e-08	3.7	0.00018	5.9	4.7e-09
10	NUDT5	CDC123,CAMK1D	Nerve-Tibial	-4.2	2.6e-05	-0.86	0.39	-3.6	0.00029
10	NUDT5	CDC123,CAMK1D	Whole-Blood-DGN	5.7	1.1e-08	3.5	0.00049	6	2e-09

Table S3 (Continued). MetaXcan associations with T2D.

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
10	HHEX	IDE,KIF11,HHEX	Cells-Transformed-fibroblasts	-6.9	5.9e-12	-3.8	0.00013	-7.1	1.2e-12
10	HHEX	IDE,KIF11,HHEX	Whole-Blood-DGN	-6.3	3.2e-10	-2.8	0.0046	-6.1	9.3e-10
10	CYP26C1	IDE,KIF11,HHEX	Adipose-Subcutaneous	-6.4	1.5e-10	-2.8	0.0053	-6.1	9.3e-10
10	CWF19L1	none reported	Breast-Mammary-Tissue	-5.5	4.6e-08	-0.76	0.45	-4.7	2.9e-06
10	TCF7L2	TCF7L2	Adrenal-Gland	4.1	3.5e-05	-0.018	0.99	3.4	0.00075
10	TCF7L2	TCF7L2	Artery-Aorta	-9.5	2.5e-21	-8.9	8.7e-19	-12	2e-31
10	ZDHHC6	TCF7L2	Adipose-Subcutaneous	-4.2	2.4e-05	-1.5	0.13	-3.9	1e-04
10	GPAM	TCF7L2	Breast-Mammary-Tissue	-5	5.6e-07	-1.5	0.14	-4.7	3e-06
10	DCLRE1A	TCF7L2	Cells-Transformed-fibroblasts	5.9	3.3e-09	5.2	2e-07	7	1.8e-12
10	DCLRE1A	TCF7L2	Thyroid	-7.4	1.1e-13	-5	4.7e-07	-8.4	4.9e-17
10	NHLRC2	TCF7L2	Cells-Transformed-fibroblasts	-4.1	3.9e-05	-3.7	0.00021	-4.9	7.7e-07
10	CASP7	TCF7L2	Spleen	4.9	9.8e-07	1.7	0.097	5	6.4e-07
10	SFTPA2	ZMIZ1	Adipose-Subcutaneous	4.1	3.7e-05	1	0.3	3.6	0.00035
11	TAF1D	MTNR1B	Brain-Nucleus-accumbens-basal-ganglia	4.2	2.9e-05	2.8	0.0056	4.7	2.2e-06
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Breast-Mammary-Tissue	-5.7	1.5e-08	-3.9	8.4e-05	-6.4	1.3e-10
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Esophagus-Mucosa	-5.4	8.4e-08	-2.8	0.0044	-5.6	2.7e-08
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Heart-Left-Ventricle	-4.9	1.2e-06	-1.7	0.088	-4.6	3.3e-06
11	NCR3LG1	NCR3LG1,KCNJ11,ABCC8	Nerve-Tibial	-5.6	2.6e-08	-3.3	0.00092	-5.8	5e-09
11	KCNJ11	NCR3LG1,KCNJ11,ABCC8	Esophagus-Mucosa	-4.6	3.6e-06	-2.9	0.004	-5	5.1e-07
11	KCNJ11	NCR3LG1,KCNJ11,ABCC8	Skin-Sun-Exposed-Lower-leg	-4.3	2e-05	-2.6	0.009	-4.5	6.1e-06
11	KCNJ11	NCR3LG1,KCNJ11,ABCC8	Whole-Blood-DGN	4.5	8.4e-06	3.5	4e-04	5.1	3.8e-07
11	TCP11L1	none reported	Muscle-Skeletal	4.1	4.3e-05	-0.24	0.81	3.1	0.0022
11	TCP11L1	none reported	Adipose-Visceral-Omentum	4.1	3.6e-05	-0.066	0.95	3.2	0.0012
11	TCP11L1	none reported	Artery-Aorta	4.4	1e-05	-0.055	0.96	3.4	0.00079
11	TCP11L1	none reported	Brain-Cerebellum	4.8	1.7e-06	0.21	0.83	3.9	7.9e-05
11	TCP11L1	none reported	Esophagus-Mucosa	4.5	6.3e-06	-0.33	0.74	3.3	0.00088
11	TCP11L1	none reported	Esophagus-Muscularis	4.9	1.2e-06	-0.52	0.6	3.5	0.00045
11	TCP11L1	none reported	Heart-Atrial-Appendage	4.7	3.2e-06	-0.31	0.76	3.5	5e-04
11	TCP11L1	none reported	Heart-Left-Ventricle	4.6	3.4e-06	-0.48	0.63	3.4	0.00071
11	TCP11L1	none reported	Pancreas	4.5	7e-06	-0.46	0.65	3.3	0.0011
11	TCP11L1	none reported	Pituitary	4.2	2.2e-05	-0.48	0.63	3.2	0.0016
11	TCP11L1	none reported	Skin-Not-Sun-Exposed-Suprapubic	4.4	1.2e-05	-0.93	0.35	2.9	0.0034
11	TCP11L1	none reported	Skin-Sun-Exposed-Lower-leg	4.6	3.8e-06	0.078	0.94	3.6	0.00038
11	TCP11L1	none reported	Thyroid	4.5	7.3e-06	0.12	0.91	3.6	0.00034
11	MAPK8IP1	none reported	Brain-Hippocampus	4.1	4.1e-05	-0.33	0.74	3.3	0.001
11	KCNK7	none reported	Lung	-4.4	1.1e-05	0.33	0.74	-3.2	0.0014
11	DEPDC7	none reported	Nerve-Tibial	-4.5	6.3e-06	0.14	0.89	-3.4	0.00077
12	P2RX4	HNF1A,OASL	Pancreas	4.2	2.3e-05	1.5	0.13	4.1	4.8e-05
12	KLHL42	KLHL42	Artery-Tibial	-4.8	1.9e-06	NA	NA	NA	NA
12	KLHL42	KLHL42	Artery-Tibial	-4.8	1.9e-06	NA	NA	NA	NA

Table S3 (Continued). MetaXcan associations with T2D.

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
12	CCDC92	MPHOSPH9	Breast-Mammary-Tissue	-4.5	6.1e-06	-0.46	0.65	-3.8	0.00016
12	C12orf65	MPHOSPH9	Esophagus-Muscularis	4.3	1.9e-05	0.62	0.54	3.6	0.00029
12	C12orf65	MPHOSPH9	Nerve-Tibial	4.8	1.5e-06	NA	NA	NA	NA
12	PXMP2	none reported	Esophagus-Muscularis	-4.4	1.2e-05	-2.3	0.019	-4.6	5.1e-06
12	DNAJC14	none reported	Uterus	-4.8	1.6e-06	-1.1	0.29	-4.6	3.3e-06
14	VIPAS39	none reported	Nerve-Tibial	-4.3	1.8e-05	0.3	0.76	-3.1	0.0019
14	VIPAS39	none reported	Skin-Sun-Exposed-Lower-leg	-4.2	3.1e-05	0.1	0.92	-3.1	0.0018
14	VIPAS39	none reported	Testis	-4.5	7.6e-06	-0.11	0.91	-3.6	0.00032
14	VIPAS39	none reported	Thyroid	-4.1	4.4e-05	-0.089	0.93	-3.3	0.0011
14	NOXRED1	none reported	Nerve-Tibial	4.4	1.2e-05	-0.028	0.98	3.3	0.00093
15	AP3S2	AP3S2,PRC1,VPS33B	Prostate	4.1	3.6e-05	3.1	0.0018	5.3	1.3e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Adipose-Subcutaneous	4.3	1.8e-05	3.8	0.00014	5	5e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Adipose-Visceral-Omentum	4.1	3.9e-05	3.7	0.00024	5.2	2.6e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Adrenal-Gland	4.8	1.7e-06	3.6	0.00033	5.8	6.4e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Artery-Aorta	4.3	1.5e-05	3.4	0.00057	5	5e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Artery-Coronary	5	7.3e-07	3.7	0.00018	5.8	7.3e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Artery-Tibial	4.4	1.1e-05	3.8	0.00012	5.3	9.1e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Brain-Anterior-cingulate-cortex-BA24	4.8	1.5e-06	3.6	0.00027	6	2.6e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Brain-Caudate-basal-ganglia	4.6	4.8e-06	3.7	2e-04	5.8	8.2e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Brain-Cortex	4.2	2.9e-05	3	0.0023	5	7.2e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Brain-Putamen-basal-ganglia	4.4	9.5e-06	3.5	0.00039	5.6	2.8e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Breast-Mammary-Tissue	4.2	2.1e-05	3.8	0.00018	5.2	1.6e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Cells-Transformed-fibroblasts	4.2	3.3e-05	3.5	0.00048	4.9	1.1e-06
15	AP3S2	AP3S2,PRC1,VPS33B	Colon-Sigmoid	4.6	5.1e-06	3.8	0.00012	5.6	2e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Colon-Transverse	4.3	2e-05	3.5	0.00054	5	4.8e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Esophagus-Mucosa	4.6	5.2e-06	3.8	0.00017	5.4	6.6e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Heart-Left-Ventricle	5	4.8e-07	3.9	9.8e-05	5.9	3.9e-09
15	AP3S2	AP3S2,PRC1,VPS33B	Liver	4.3	1.5e-05	3.6	3e-04	5.2	2e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Nerve-Tibial	4.7	2.7e-06	3.7	0.00019	5.4	6.9e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Ovary	4.7	2.8e-06	3.5	0.00046	5.5	3.7e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Pancreas	4.5	8.1e-06	3.6	0.00032	5.3	1.2e-07
15	AP3S2	AP3S2,PRC1,VPS33B	Skin-Sun-Exposed-Lower-leg	4.8	1.4e-06	3.7	0.00022	5.5	4.1e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Small-Intestine-Terminal-Ileum	5.2	1.9e-07	3.5	0.00046	6.3	2.2e-10
15	AP3S2	AP3S2,PRC1,VPS33B	Stomach	4.9	1.1e-06	3.5	0.00047	5.7	1.3e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Thyroid	4.8	1.7e-06	3.7	0.00023	5.6	1.9e-08
15	AP3S2	AP3S2,PRC1,VPS33B	Uterus	4.8	1.5e-06	3.6	0.00035	6	1.6e-09
15	PRC1	AP3S2,PRC1,VPS33B	Pancreas	-4.7	3.1e-06	-2.9	0.0037	-5.1	3.5e-07
15	PRC1	AP3S2,PRC1,VPS33B	Whole-Blood-DGN	-4.4	1.1e-05	-2.1	0.033	-4.3	1.4e-05
15	VPS33B	AP3S2,PRC1,VPS33B	Pituitary	5	5.1e-07	1.8	0.077	5	7e-07
15	VPS33B	AP3S2,PRC1,VPS33B	Testis	-4.9	1.1e-06	-2.3	0.023	-5	5.1e-07

Table S3 (Continued). MetaXcan associations with T2D.

Chr	Gene	Reported Genes within 1Mb Locus	Model	DIAGRAM Z-score	DIAGRAM P-value	GERA Z-score	GERA P-value	Meta-analysis Z-score	Meta-analysis P-value
15	VPS33B	AP3S2,PRC1,VPS33B	Whole-Blood	-4.4	9.3e-06	-1	0.3	-3.9	8.2e-05
15	VPS33B	AP3S2,PRC1,VPS33B	Whole-Blood-DGN	-4.3	2.1e-05	-1.5	0.14	-3.9	8.5e-05
15	RCCD1	AP3S2,PRC1,VPS33B	Adipose-Subcutaneous	5	4.8e-07	3.1	0.0018	5.3	1.5e-07
15	RCCD1	AP3S2,PRC1,VPS33B	Adipose-Visceral-Omentum	4.7	3.3e-06	2.5	0.013	5	7e-07
15	RCCD1	AP3S2,PRC1,VPS33B	Artery-Aorta	5.4	6e-08	3.1	0.0022	5.7	1.4e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Artery-Coronary	4.6	3.7e-06	2.4	0.015	4.9	1.1e-06
15	RCCD1	AP3S2,PRC1,VPS33B	Artery-Tibial	5.3	1.5e-07	3.4	0.00077	5.8	7.8e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Anterior-cingulate-cortex-BA24	5	5.7e-07	3.1	0.0019	5.8	5.8e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Caudate-basal-ganglia	4.8	1.8e-06	2.5	0.014	5.3	1.5e-07
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Cerebellar-Hemisphere	4.8	1.5e-06	2.9	0.0032	5.5	4.1e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Cerebellum	5	5.8e-07	3.4	0.00069	5.8	8.5e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Cortex	5.7	1.4e-08	3.1	0.0018	6.2	5.7e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Brain-Frontal-Cortex-BA9	5.7	1.5e-08	3	0.0031	6.3	2.7e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Breast-Mammary-Tissue	5.2	1.6e-07	2.7	0.0079	5.5	4.9e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Cells-Transformed-fibroblasts	4.4	1e-05	1.9	0.052	4.3	1.7e-05
15	RCCD1	AP3S2,PRC1,VPS33B	Colon-Sigmoid	5.5	4.9e-08	2.6	0.0097	5.7	1.3e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Colon-Transverse	5.5	4.9e-08	3.2	0.0013	5.8	5.5e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Esophagus-Gastroesophageal-Junction	5.4	5.1e-08	2.4	0.015	5.7	1.4e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Esophagus-Mucosa	5	4.6e-07	3.1	0.002	5.4	5.3e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Heart-Left-Ventricle	4.8	1.9e-06	2.1	0.035	4.8	1.8e-06
15	RCCD1	AP3S2,PRC1,VPS33B	Muscle-Skeletal	4.6	4.4e-06	2.7	0.0065	4.9	7.9e-07
15	RCCD1	AP3S2,PRC1,VPS33B	Nerve-Tibial	5.5	3e-08	3.2	0.0014	5.8	7.9e-09
15	RCCD1	AP3S2,PRC1,VPS33B	Skin-Not-Sun-Exposed-Suprapubic	5.2	1.8e-07	3	0.0027	5.6	2.8e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Skin-Sun-Exposed-Lower-leg	5.2	2.2e-07	3.1	0.0019	5.5	4.5e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Stomach	5.7	1.4e-08	3.2	0.0012	6.2	6.1e-10
15	RCCD1	AP3S2,PRC1,VPS33B	Testis	5.2	2.1e-07	3.2	0.0015	5.7	1e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Thyroid	5	6.3e-07	3	0.0027	5.4	5.6e-08
15	RCCD1	AP3S2,PRC1,VPS33B	Whole-Blood-DGN	4.8	1.9e-06	3	0.0028	5	4.5e-07
15	PP1B	none reported	Testis	-5.1	3.7e-07	-2.2	0.027	-5.2	2.6e-07
15	HMG20A	PEAK1,HMG20A,LINGO1	Pituitary	5.5	4.5e-08	3.4	0.00065	6.2	6.7e-10
15	HMG20A	PEAK1,HMG20A,LINGO1	Vagina	-4.1	4.1e-05	-0.81	0.42	-4	6.9e-05
15	RCN2	PEAK1,HMG20A,LINGO1	Colon-Transverse	4.6	3.7e-06	3.1	0.0022	5.1	3.2e-07
15	ZFAND6	ZFAND6	Brain-Cerebellar-Hemisphere	4.5	6e-06	-1.7	0.096	2.8	0.0048
15	ZFAND6	ZFAND6	Brain-Cortex	-4.1	4.1e-05	1.3	0.19	-2.6	0.0085
15	FAH	ZFAND6	Brain-Cerebellum	4.2	3.3e-05	-1.2	0.24	2.7	0.0064
16	ZNF771	none reported	Brain-Hippocampus	-4.7	3.2e-06	-2	0.044	-5	4.8e-07
16	HSDL1	none reported	Liver	-4.1	4.1e-05	0.93	0.35	-2.7	0.0063
17	COP22	none reported	Adipose-Subcutaneous	4.3	1.8e-05	-0.11	0.91	3.2	0.0016
17	SNX11	none reported	Brain-Cerebellar-Hemisphere	4.1	3.4e-05	0.91	0.36	3.9	0.00011
17	SNX11	none reported	Thyroid	4.1	4.2e-05	0.18	0.86	3.3	0.00094
17	SPATA20	none reported	Esophagus-Gastroesophageal-Junction	4.3	1.7e-05	0.63	0.53	3.8	0.00014
19	CNN1	none reported	Brain-Nucleus-accumbens-basal-ganglia	5.1	3.7e-07	-0.75	0.45	3.6	0.00027
19	JUND	none reported	Cells-Transformed-fibroblasts	4.2	2.2e-05	NA	NA	NA	NA
19	JUND	none reported	Skin-Sun-Exposed-Lower-leg	4.4	1.4e-05	NA	NA	NA	NA
19	JUND	none reported	Whole-Blood	4.5	7.7e-06	NA	NA	NA	NA
22	XBP1	none reported	Brain-Cerebellum	-4.2	3.2e-05	-1.5	0.14	-4.1	4.2e-05
22	MKL1	none reported	Skin-Sun-Exposed-Lower-leg	-4.3	1.9e-05	-0.88	0.38	-3.7	0.00022

Table S3 (Continued). MetaXcan associations with T2D.

Rank	GO:BP Pathway	P-value
1	negative regulation of type B pancreatic cell apoptotic process	0.0001
2	protein destabilization	0.0003
3	regulation of type B pancreatic cell apoptotic process	0.001
4	type B pancreatic cell apoptotic process	0.001
5	response to fructose	0.001
6	positive regulation of cellular biosynthetic process	0.001
7	positive regulation of nitrogen compound metabolic process	0.001
8	positive regulation of biosynthetic process	0.001
9	ATF6-mediated unfolded protein response	0.001
10	positive regulation of transcription, DNA-templated	0.001
11	positive regulation of nucleic acid-templated transcription	0.001
12	positive regulation of nucleobase-containing compound metabolic process	0.001
13	positive regulation of RNA biosynthetic process	0.002
14	negative regulation of endoplasmic reticulum unfolded protein response	0.002
15	fatty acid homeostasis	0.002
16	positive regulation of triglyceride biosynthetic process	0.002
17	positive regulation of RNA metabolic process	0.002
18	negative regulation of apoptotic signaling pathway	0.002
19	stabilization of membrane potential	0.003
20	regulation of epithelial cell apoptotic process	0.003

Table S4. Gene set enrichment analysis of genes corresponding to tissue-level associations at $FDR \leq 0.05$. The top 20 Gene Ontology Biological Process (GO:BP) pathways enriched among the set of MetaXcan-significant genes are shown with overrepresented p-value.

Rank	GO:BP Pathway	P-value
1	regulation of type B pancreatic cell apoptotic process	0.0001
2	negative regulation of type B pancreatic cell apoptotic process	0.0001
3	type B pancreatic cell apoptotic process	0.0002
4	regulation of cyclin-dependent protein serine/threonine kinase activity	0.0004
5	negative regulation of sequence-specific DNA binding transcription factor activity	0.001
6	regulation of protein export from nucleus	0.001
7	negative regulation of cyclin-dependent protein serine/threonine kinase activity	0.001
8	negative regulation of epithelial cell apoptotic process	0.001
9	hepatic duct development	0.001
10	hepatoblast differentiation	0.001
11	regulation of cyclin-dependent protein kinase activity	0.001
12	positive regulation of nucleobase-containing compound metabolic process	0.001
13	regulation of sequence-specific DNA binding transcription factor activity	0.001
14	canonical Wnt signaling pathway involved in positive regulation of epithelial to mesenchymal transition	0.001
15	positive regulation of cellular biosynthetic process	0.002
16	negative regulation of ATF6-mediated unfolded protein response	0.002
17	negative regulation of cellular macromolecule biosynthetic process	0.002
18	positive regulation of biosynthetic process	0.002
19	nuclear export	0.002
20	positive regulation of nitrogen compound metabolic process	0.002

Table S5. Gene set enrichment analysis of *reported* T2D genes corresponding to tissue-level associations at $FDR \leq 0.05$. The top 20 Gene Ontology Biological Process (GO:BP) pathways enriched among the set of MetaXcan-significant genes are shown with overrepresented p-value.

Rank	GO:BP Pathway	P-value
1	response to fructose	0.001
2	fatty acid homeostasis	0.001
3	stabilization of membrane potential	0.001
4	embryonic skeletal joint development	0.001
5	menaquinone biosynthetic process	0.004
6	vitamin K biosynthetic process	0.004
7	epithelial cell differentiation involved in salivary gland development	0.004
8	epithelial cell maturation involved in salivary gland development	0.004
9	positive regulation of phospholipid biosynthetic process by transcription from RNA polymerase II promoter	0.004
10	regulation of plasma cell differentiation	0.004
11	positive regulation of plasma cell differentiation	0.004
12	positive regulation of phospholipid biosynthetic process by positive regulation of transcription from RNA polymerase II promoter	0.004
13	regulation of lactation	0.004
14	positive regulation of lactation	0.004
15	negative regulation of activation-induced cell death of T cells	0.005
16	protein destabilization	0.006
17	positive regulation of multicellular organism growth	0.007
18	response to fluid shear stress	0.008
19	rescue of stalled ribosome	0.008
20	adenine transport	0.008

Table S6. Gene set enrichment analysis of *novel* T2D genes corresponding to tissue-level associations at $FDR \leq 0.05$. The top 20 Gene Ontology Biological Process (GO:BP) pathways enriched among the set of MetaXcan-significant genes are shown with overrepresented p-value.

Trait	P-value	Reported T2D Genes	Novel Genes
Type 2 diabetes	0.0001	<i>IGF2BP2, WFS1, PCBD2</i> <i>ETV1, JAZF1, INTS8</i> <i>TP53INP1, HHEX, TCF7L2</i> <i>KCNJ11, HMG20A, ZFAND6</i> <i>AP3S2, PRC1</i>	
Type 2 diabetes and other traits	0.0002	<i>WFS1, TCF7L2</i>	
Fasting glucose-related traits (interaction with BMI)	0.001	<i>IGF2BP2, TCF7L2</i>	
Free thyroxine concentration	0.002	<i>JAZF1</i>	
Height	0.002	<i>IGF2BP2, TXNDC15, PCBD2</i> <i>JAZF1</i>	
Colorectal cancer	0.002	<i>PCBD2, TCF7L2</i>	
Breast Cancer in BRCA1 mutation carriers	0.003	<i>TCF7L2</i>	
Diabetes (gestational)	0.005	<i>IGF2BP2</i>	
Vincristine-induced peripheral neuropathy in acute lymphoblastic leukemia	0.006	<i>NDUFAF6</i>	
Two-hour glucose challenge	0.007	<i>TCF7L2</i>	
Breast cancer	0.008	<i>TCF7L2, PRC1</i>	
Dehydroepiandrosterone sulphate levels	0.012	<i>HHEX</i>	
Proinsulin levels	0.013	<i>TCF7L2</i>	
IgE levels	0.019	<i>HCG27</i>	
Fasting glucose-related traits	0.021	<i>TCF7L2</i>	
Fasting insulin-related traits (interaction with BMI)	0.023	<i>TCF7L2</i>	
Systemic lupus erythematosus and Systemic sclerosis	0.023	<i>JAZF1</i>	
Lupus nephritis in systemic lupus erythematosus	0.024	<i>HCG27</i>	
Social communication problems	0.025	<i>KCNJ11</i>	
Glycated hemoglobin levels	0.028	<i>TCF7L2</i>	
Bulimia nervosa	0.030	<i>PCBD2</i>	
Metabolic syndrome	0.047	<i>TCF7L2</i>	

Table S7. Enrichment of reported T2D genes identified in MetaXcan among the set of reported genes from GWAS of other phenotypes. Tissue-level gene associations at $FDR \leq 0.05$ corresponding to reported T2D genes based on proximity to T2D-associated SNPs from the trans-ethnic meta-analysis were tested for enrichment among the set of reported genes from all traits in the NHGRI-EBI online catalogue of GWAS results.

Trait	P-value	Reported T2D Genes	Novel Genes
Epilepsy (generalized)	0.0001		<i>COPZ2, SNX11</i> <i>MAST4</i>
Waist-to-hip ratio adjusted for body mass index	0.0004		<i>CCDC92, HOXA11</i> <i>MEIS1, JUND</i>
Esophageal squamous cell carcinoma	0.001	<i>CDKN2A</i>	<i>XBP1</i>
Endometriosis	0.004	<i>CDKN2A</i>	<i>ID4</i>
Drug-induced liver injury (amoxicillin-clavulanate)	0.005		<i>HLA-A</i>
Bronchodilator response in asthma	0.007		<i>JUND</i>
Urate levels in obese individuals	0.012		<i>EXT1, MED30</i>
Change in intraocular pressure in response to steroid treatment (triamcinolone acetonide)	0.012		<i>HLA-A</i>
Abdominal aortic aneurysm	0.014	<i>CDKN2A</i>	
Vitiligo	0.016		<i>CASP7, HLA-A</i>
Treatment response for severe sepsis	0.017		<i>MKL1</i>
Vincristine-induced peripheral neuropathy in acute lymphoblastic leukemia	0.020		<i>ETAA1</i>
Age-related macular degeneration (CNV)	0.022		<i>C2</i>
Restless legs syndrome	0.024		<i>MEIS1</i>
Circulating myeloperoxidase levels (serum)	0.025		<i>C2</i>
Type 2 diabetes	0.026	<i>CDKN2A, CAMK1D</i> <i>THADA</i>	
Glioma	0.027	<i>CDKN2A</i>	
Esophageal cancer (squamous cell)	0.028		<i>XBP1</i>
Milk allergy	0.028		<i>ETAA1</i>
Myocardial infarction	0.029	<i>CDKN2A</i>	
Nasopharyngeal carcinoma	0.030		<i>HLA-A</i>
Hair morphology	0.031	<i>THADA</i>	
Carotid atherosclerosis in HIV infection	0.031		<i>MAST4</i>
Platelet count	0.031	<i>CDKN2A, THADA</i>	
Cutaneous lupus erythematosus	0.037		<i>TRIM39</i>
QT interval (interaction)	0.038	<i>CAMK1D</i>	
Glycemic traits (pregnancy)	0.044		<i>HKDC1</i>
Intracranial aneurysm	0.045	<i>CDKN2A</i>	
Colorectal cancer (diet interaction)	0.048		<i>MEIS1</i>
PR segment	0.049		<i>MEIS1</i>

Table S8. Enrichment of *novel* T2D genes identified in MetaXcan among the set of reported genes from GWAS of other phenotypes. Tissue-level gene associations at FDR ≤ 0.05 corresponding to novel T2D genes (exceeding 1 Mb from T2D-associated SNPs from the trans-ethnic meta-analysis) were tested for enrichment among the set of reported genes from all traits in the NHGRI-EBI online catalogue of GWAS results.

Chr	Region Start	Region End	Reported Genes	Genome-significant Genes	Genome-significant Models	Region-significant Genes	Region-significant Models
2	59678302	61780702	BCL11A	NA	NA	BCL11A	Pancreas
2	225265364	228664475	NYAP2, IRS1	NA	NA	IRS1	Adipose.Subcutaneous
3	58735036	62237194	FHIT	NA	NA	FHIT	Whole.Blood
3	184361527	189608460	C3orf65, IGF2BP2, ST6GAL1, LPP	IGF2BP2	Thyroid	SENP2, ST6GAL1	Adrenal.Gland, Ovary
4	5271576	7565327	WFS1, PPP2R2C	WFS1, WFS1, WFS1, WFS1	Brain.Cerebellum, Nerve.Tibial, Skin.Not.Sun.Exposed.Suprapubic, Skin.Sun.Exposed.Lower.leg, Thyroid	EVC, WFS1, WFS1, WFS1, WFS1	Spleen, Brain.Caudate.basal.ganglia, Brain.Cerebellar.Hemisphere, Cells.Transform.ed.fibroblasts, Heart.Left.Ventricle, Muscle.Skeletal
5	133209493	135343649	TXNDC15, PCBD2	NA	NA	PCBD2, PCBD2, SAR1B, TXNDC15, TXNDC15, TXNDC15, TXNDC15	Breast.Mammary.Tissue, Whole.Blood.DGN, Liver, Adipose.Subcutaneous, Artery.Aorta, Artery.Tibial, Esophagus.Mucosa
5	167088745	169728133	SLIT3	NA	NA	SLIT3	Testis
6	19534688	22232635	CDKAL1	ID4	Vagina	SOX4	Muscle.Skeletal
6	30103949	32210949	CCHCR1, TCF19, POU5F1, HCG27	NA	NA	C2, CYP21A2, DHX16, HCG27, HCG27, HCG27, HCG27, TRIM39	Adipose.Subcutaneous, Adipose.Visceral.Omentum, Brain.Cerebellar.Hemisphere, Adipose.Subcutaneous, Artery.Tibial, Colon.Sigmoid, Lung, Spleen, Whole.Blood
6	125661320	127670021	CENPW	NA	NA	CENPW, RNF146	Brain.Cortex, Adipose.Visceral.Omentum
7	12930853	16014402	ETV1, DGKB	NA	NA	ETV1	Cells.Transform.ed.fibroblasts
7	26870192	29220362	JAZF1	JAZF1, JAZF1, JAZF1, JAZF1, JAZF1	Adipose.Subcutaneous, Adipose.Visceral.Omentum, Artery.Aorta, Artery.Tibial, Cells.Transform.ed.fibroblasts, Muscle.Skeletal, Pancreas	HGX11	Colon.Sigmoid
8	40510739	42754280	ANK1	NA	NA	VDAC3	Adrenal.Gland
8	94731931	97126883	DPY19L4, INTS8, CCNE2, TP53INP1, NDUFAF6	CCNE2, TP53INP1, TP53INP1, TP53INP1	Whole.Blood.DGN, Skin.Sun.Exposed.Lower.leg, Testis, Whole.Blood.DGN	CCNE2, CCNE2, CCNE2, DPY19L4, INTS8, NDUFAF6, NDUFAF6, NDUFAF6	Adipose.Visceral.Omentum, Cells.EBV-transformed.lymphocytes, Lung, Testis, Heart.Atrial.Appendage, Artery.Tibial, Whole.Blood.DGN, Brain.Cerebellar.Hemisphere, Brain.Cerebellum, Cells.Transform.ed.fibroblasts, Ovary, Whole.Blood
8	116962512	119188953	SLC30A8	NA	NA	EIF3H, EXT1, MED30, RAD21	Pancreas, Brain.Caudate.basal.ganglia, Brain.Hippocampus, Vagina
9	21002902	23455739	CDKN2B, DMRTA1	CDKN2A	Adrenal.Gland	KLHL9	Brain.Hypothalamus
10	11237964	13292588	CDC123	CAMK1D, CAMK1D, NUDT5	Whole.Blood, Whole.Blood.DGN, Whole.Blood.DGN	CAMK1D, CAMK1D, CAMK1D, NUDT5, NUDT5	Heart.Atrial.Appendage, Heart.Left.Ventricle, Lung, Nerve.Tibial, Skin.Sun.Exposed.Lower.leg
10	70390007	72452208	C10orf35, RP11-242G20.1	NA	NA	HKDC1, HKDC1	Artery.Aorta, Esophagus.Mucosa
10	79828792	82076276	ZMIZ1	NA	NA	PIPF, SFTPA2	Esophagus.Gastroesophageal.Junction, Adipose.Subcutaneous
10	93211441	95455403	IDE, KIF11, HHEX	HHEX, HHEX, CYP28C1	Cells.Transform.ed.fibroblasts, Whole.Blood.DGN, Adipose.Subcutaneous	NA	NA
10	113710009	115927437	TCF7L2	TCF7L2, DCLRE1A, DCLRE1A	Artery.Aorta, Cells.Transform.ed.fibroblasts, Thyroid	CASP7, CASP7, GPAM, GPAM, NHLRC2, TCF7L2, ZDHHC6, ZDHHC6	Artery.Aorta, Spleen, Breast.Mammary.Tissue, Ovary, Cells.Transform.ed.fibroblasts, Adrenal.Gland, Adipose.Subcutaneous, Muscle.Skeletal
11	1465914	3870339	KCNQ1	NA	NA	CARS, INS, KCNQ1, SYT8	Adipose.Subcutaneous, Nerve.Tibial, Prostate, Prostate
11	16373273	18498449	NCR3LG1, KCNJ11, ABCC8	NCR3LG1, NCR3LG1, NCR3LG1	Breast.Mammary.Tissue, Esophagus.Mucosa, Nerve.Tibial	ABCC8, KCNJ11, KCNJ11, KCNJ11, NCR3LG1	Brain.Cortex, Esophagus.Mucosa, Skin.Sun.Exposed.Lower.leg, Whole.Blood.DGN, Heart.Left.Ventricle
11	71396114	73853306	ARAP1, STARD10, ATG16L2, FCHSD2	NA	NA	STARD10	Whole.Blood.DGN
11	91702886	93718232	MTNR1B	NA	NA	TAF1D	Brain.Nucleus.accumbens.basal.ganglia
12	26932953	28955973	KLHL42	NA	NA	KLHL42	Artery.Tibial
12	70518865	72835678	TSPAN8	NA	NA	CTD-2021H9.3, CTD-2021H9.3, TSPAN8	Colon.Transverse, Muscle.Skeletal, Liver
12	120418346	122477045	HNF1A, OASL	NA	NA	C12orf43, CABP1, P2RX4	Brain.Anterior.cingulate.cortex.BA24, Adipose.Subcutaneous, Pancreas

Table S9. Genome-wide and window-level significant gene associations at regions spanning T2D-associated loci.

Chr	Region Start	Region End	Reported Genes	Genome-significant Genes	Genome-significant Models	Region-significant Genes	Region-significant Models
12	122836867	124728561	MPHOSPH9	NA	NA	C12orf65, C12orf65 CCDC82, CDK2AP1 MPHOSPH9	Esophagus.Muscularis, Nerve.Tibial Breast.Mammary.Tissue, Nerve.Tibial Artery.Tibial
15	61359176	63457482	C2CD4A, C2CD4B	NA	NA	C2CD4A	Nerve.Tibial
15	76400471	79113242	PEAK1, HMG20A LINGO1	HMG20A	Pituitary	HMG20A, HMG20A LINGO1, RCN2	Muscle.Skeletal, Vagina Brain.Putamen.basal.ganglia, Colon.Transverse
15	79351910	81430735	ZFAND6	NA	NA	FAH, ZFAND6 ZFAND6	Brain.Cerebellum, Brain.Cerebellar.Hemisphere Brain.Cortex
15	89373831	92565833	AP3S2, PRC1 VPS33B	AP3S2, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1	Small Intestine.Terminal.Ileum, Artery.Aorta Artery.Tibial, Brain.Cortex Brain.Frontal.Cortex.BA9, Breast.Mammary.Tissue Colon.Sigmoid, Colon.Transverse Esophagus.Gastroesophageal.Junction, Nerve.Tibial Skin.Not.Sun.Exposed.Suprapubic, Skin.Sun.Exposed.Lower.Leg Stomach, Testis	AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, AP3S2 AP3S2, PRC1 PRC1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 RCCD1, RCCD1 UNC45A, VPS33B VPS33B, VPS33B VPS33B	Adipose.Subcutaneous, Adipose.Visceral.Omentum Adrenal.Gland, Artery.Aorta Artery.Coronary, Artery.Tibial Brain.Anterior.cingulate.cortex.BA9, Brain.Caudate.basal.ganglia Brain.Cortex, Brain.Frontal.Cortex.BA9 Brain.Nucleus.accumbens.basal.ganglia, Brain.Putamen.basal.ganglia Breast.Mammary.Tissue, Cells.EBV-transformed.lymphocytes Cells.Transformed.fibroblasts, Colon.Sigmoid Colon.Transverse, Esophagus.Mucosa Esophagus.Muscularis, Heart.Left.Ventricle Liver, Nerve.Tibial Ovary, Pancreas Prostate, Skin.Sun.Exposed.Lower.leg Stomach, Thyroid Uterus, Pancreas Whole.Blood.DGN, Adipose.Subcutaneous Adipose.Visceral.Omentum, Artery.Coronary Brain.Anterior.cingulate.cortex.BA24, Brain.Caudate.basal.ganglia Brain.Cerebellar.Hemisphere, Brain.Cerebellum Brain.Nucleus.accumbens.basal.ganglia, Cells.Transformed.fibroblasts Esophagus.Mucosa, Esophagus.Muscularis Heart.Left.Ventricle, Muscle.Skeletal Thyroid, Whole.Blood.DGN Muscle.Skeletal, Pituitary Testis, Whole.Blood Whole.Blood.DGN

Table S9 (Continued). Genome-wide and window-level significant gene associations at regions spanning T2D-associated loci.

Chr	Gene	Model	DIAGRAM Z-score	DIAGRAM p-value	GERA Z-score	GERA p-value
2	BCL11A	Pancreas	3.95	7.82e-05	1.49	0.137
2	IRS1	Adipose-Subcutaneous	-3.74	0.000181	-3.22	0.00129
3	FHIT	Whole-Blood	-2.91	0.00357	-1.78	0.0751
3	IGF2BP2	Thyroid	7.46	8.58e-14	5.86	4.77e-09
3	SENP2	Adrenal-Gland	5.08	3.73e-07	0.501	0.616
3	ST6GAL1	Ovary	3.86	0.000114	0.793	0.428
4	EVC	Spleen	5.06	4.13e-07	3.7	0.000219
4	WFS1	Brain-Caudate-basal-ganglia	-3.75	0.00018	-3.53	0.000421
4	WFS1	Brain-Cerebellar-Hemisphere	4.56	5.03e-06	4	6.41e-05
4	WFS1	Brain-Cerebellum	5.24	1.62e-07	3.88	0.000106
4	WFS1	Cells-Transformed-fibroblasts	4.36	1.29e-05	3.17	0.00154
4	WFS1	Heart-Left-Ventricle	4.24	2.27e-05	2.72	0.00661
4	WFS1	Muscle-Skeletal	3.67	0.000244	3.94	8.28e-05
4	WFS1	Nerve-Tibial	5.5	3.72e-08	4.51	6.48e-06
4	WFS1	Skin-Not-Sun-Exposed-Suprapubic	5.26	1.43e-07	5.01	5.54e-07
4	WFS1	Skin-Sun-Exposed-Lower-leg	5.72	1.08e-08	4.58	4.72e-06
4	WFS1	Thyroid	5.37	7.79e-08	4.75	2.08e-06
5	PCBD2	Breast-Mammary-Tissue	-3.69	0.000223	-1.9	0.0571
5	PCBD2	Whole-Blood-DGN	-4.56	5.05e-06	-1.75	0.0807
5	SAR1B	Liver	4.14	3.51e-05	0.0889	0.929
5	TXNDC15	Adipose-Subcutaneous	5.03	4.92e-07	1.33	0.182
5	TXNDC15	Artery-Aorta	3.74	0.000181	1.64	0.1
5	TXNDC15	Artery-Tibial	4.36	1.28e-05	1.7	0.0883
5	TXNDC15	Esophagus-Mucosa	4.38	1.16e-05	2.65	0.00806
5	SLIT3	Testis	3.86	0.000115	0.187	0.851
6	ID4	Vagina	-6.18	6.32e-10	-4.72	2.39e-06
6	SOX4	Muscle-Skeletal	-3.89	1e-04	-2.94	0.00332
6	C2	Adipose-Subcutaneous	4.32	1.53e-05	3.49	0.000489
6	CYP21A2	Adipose-Visceral-Omentum	4.08	4.46e-05	1.99	0.0465
6	DHX16	Brain-Cerebellar-Hemisphere	4.17	2.98e-05	1.72	0.085
6	HCG27	Adipose-Subcutaneous	4.32	1.53e-05	1.19	0.236
6	HCG27	Artery-Tibial	4.15	3.25e-05	1.29	0.196
6	HCG27	Colon-Sigmoid	4.17	3.1e-05	1.21	0.226
6	HCG27	Lung	4.12	3.78e-05	1.44	0.15
6	HCG27	Spleen	4.7	2.6e-06	1.29	0.197
6	TRIM39	Whole-Blood	5.08	3.73e-07	1.21	0.225
6	CENPW	Brain-Cortex	-3.61	0.00031	-2.79	0.00531
6	RNF146	Adipose-Visceral-Omentum	-3.62	0.000297	-1.64	0.101
7	ETV1	Cells-Transformed-fibroblasts	-5.11	3.26e-07	-1.1	0.27
7	HOXA11	Colon-Sigmoid	4.76	1.97e-06	3.15	0.00161

Table S10. Summary table of tissue-level gene associations at regions spanning T2D-associated loci. MetaXcan Z-scores and *p*-values for all genome-wide and window-level significant gene associations from the discovery analysis (i.e. trans-ethnic study) and GERA replication study are shown. Blue shading indicates *novel* T2D genes. Red shading indicates associations replicating in the GERA study at *p* < 0.05.

Chr	Gene	Model	DIAGRAM Z-score	DIAGRAM p-value	GERA Z-score	GERA p-value
7	JAZF1	Adipose-Subcutaneous	-6.96	3.29e-12	-6.81	9.78e-12
7	JAZF1	Adipose-Visceral-Omentum	-8.15	3.68e-16	-5.83	5.46e-09
7	JAZF1	Artery-Aorta	-5.86	4.72e-09	-4.75	2.05e-06
7	JAZF1	Artery-Tibial	-7.23	4.78e-13	-6.75	1.48e-11
7	JAZF1	Cells-Transformed-fibroblasts	-6.97	3.13e-12	-3.85	0.000117
7	JAZF1	Muscle-Skeletal	-8.47	2.49e-17	-5.58	2.4e-08
7	JAZF1	Pancreas	-7.05	1.8e-12	-5.53	3.17e-08
8	VDAC3	Adrenal-Gland	-4.76	1.97e-06	-1.34	0.182
8	CCNE2	Adipose-Visceral-Omentum	-3.92	8.79e-05	-1.85	0.0647
8	CCNE2	Cells-EBV-transformed-lymphocytes	4.06	4.99e-05	0.69	0.49
8	CCNE2	Lung	-4.6	4.22e-06	-0.773	0.439
8	CCNE2	Testis	4.47	7.99e-06	0.61	0.542
8	CCNE2	Whole-Blood-DGN	-5.54	3.03e-08	-1.02	0.309
8	DPY19L4	Heart-Atrial-Appendage	-3.62	0.000297	0.216	0.829
8	INTS8	Artery-Tibial	-4.78	1.76e-06	-1.61	0.108
8	INTS8	Whole-Blood-DGN	-5.04	4.76e-07	-1.1	0.27
8	NDUFAF6	Brain-Cerebellar-Hemisphere	-3.93	8.47e-05	-1.15	0.25
8	NDUFAF6	Brain-Cerebellum	-3.8	0.000144	-0.298	0.766
8	NDUFAF6	Cells-Transformed-fibroblasts	-4.52	6.05e-06	-1.24	0.216
8	NDUFAF6	Ovary	-3.72	0.000196	-0.28	0.78
8	TP53INP1	Skin-Sun-Exposed-Lower-leg	-5.3	1.16e-07	-0.433	0.665
8	TP53INP1	Testis	-5.4	6.85e-08	-0.573	0.566
8	TP53INP1	Whole-Blood	4	6.4e-05	1.08	0.281
8	TP53INP1	Whole-Blood-DGN	5.21	1.9e-07	0.982	0.326
8	EIF3H	Pancreas	-3.76	0.000172	-1.28	0.201
8	EXT1	Brain-Caudate-basal-ganglia	-4.51	6.5e-06	-2.58	0.00995
8	MED30	Brain-Hippocampus	4.59	4.46e-06	0.821	0.412
8	RAD21	Vagina	-4.27	1.96e-05	-1.69	0.0913
9	CDKN2A	Adrenal-Gland	-5.71	1.1e-08	-2.97	0.00296
9	KLHL9	Brain-Hypothalamus	3.94	8.19e-05	0.988	0.323
10	CAMK1D	Heart-Atrial-Appendage	4.99	6.2e-07	2.46	0.014
10	CAMK1D	Heart-Left-Ventricle	4.43	9.29e-06	3.35	0.000813
10	CAMK1D	Lung	4.41	1.02e-05	0.335	0.737
10	CAMK1D	Whole-Blood	5.97	2.42e-09	3.4	0.000664
10	CAMK1D	Whole-Blood-DGN	5.35	8.87e-08	3.75	0.000177
10	NUDT5	Nerve-Tibial	-4.21	2.57e-05	-0.865	0.387
10	NUDT5	Skin-Sun-Exposed-Lower-leg	-3.69	0.000221	-1.64	0.102
10	NUDT5	Whole-Blood-DGN	5.71	1.13e-08	3.48	0.000494
10	HKDC1	Artery-Aorta	-4.43	9.29e-06	-2.26	0.0235
10	HKDC1	Esophagus-Mucosa	-3.9	9.72e-05	1.82	0.0681

Table S10 (Continued). Summary table of tissue-level gene associations at regions spanning T2D-associated loci.

Chr	Gene	Model	DIAGRAM Z-score	DIAGRAM p-value	GERA Z-score	GERA p-value
10	PPIF	Esophagus-Gastroesophageal-Junction	3.78	0.000156	-0.47	0.639
10	SFTPA2	Adipose-Subcutaneous	4.13	3.67e-05	1.03	0.302
10	CYP26C1	Adipose-Subcutaneous	-6.4	1.51e-10	-2.79	0.00526
10	HHEX	Cells-Transformed-fibroblasts	-6.88	5.87e-12	-3.82	0.000131
10	HHEX	Whole-Blood-DGN	-6.29	3.21e-10	-2.83	0.00461
10	CASP7	Artery-Aorta	3.6	0.000315	1.89	0.0591
10	CASP7	Spleen	4.9	9.82e-07	1.66	0.0967
10	DCLRE1A	Cells-Transformed-fibroblasts	5.92	3.29e-09	5.2	2.03e-07
10	DCLRE1A	Thyroid	-7.43	1.07e-13	-5.04	4.67e-07
10	GPAM	Breast-Mammary-Tissue	-5	5.61e-07	-1.47	0.141
10	GPAM	Ovary	4.05	5.2e-05	3.65	0.00026
10	NHLRC2	Cells-Transformed-fibroblasts	-4.11	3.88e-05	-3.7	0.000214
10	TCF7L2	Adrenal-Gland	4.14	3.52e-05	-0.018	0.986
10	TCF7L2	Artery-Aorta	-9.48	2.5e-21	-8.85	8.7e-19
10	ZDHHC6	Adipose-Subcutaneous	-4.23	2.38e-05	-1.52	0.129
10	ZDHHC6	Muscle-Skeletal	-3.97	7.1e-05	-0.124	0.901
11	CARS	Adipose-Subcutaneous	3.84	0.000124	-0.673	0.501
11	INS	Nerve-Tibial	-3.91	9.05e-05	-0.599	0.549
11	KCNQ1	Prostate	3.98	6.91e-05	0.482	0.63
11	SYT8	Prostate	3.9	9.67e-05	-0.109	0.913
11	ABCC8	Brain-Cortex	-3.88	0.000103	-1.4	0.16
11	KCNJ11	Esophagus-Mucosa	-4.64	3.56e-06	-2.88	0.00397
11	KCNJ11	Skin-Sun-Exposed-Lower-leg	-4.26	2.04e-05	-2.61	0.00896
11	KCNJ11	Whole-Blood-DGN	4.45	8.39e-06	3.54	0.000403
11	NCR3LG1	Breast-Mammary-Tissue	-5.66	1.54e-08	-3.93	8.43e-05
11	NCR3LG1	Esophagus-Mucosa	-5.36	8.4e-08	-2.85	0.00444
11	NCR3LG1	Heart-Left-Ventricle	-4.86	1.2e-06	-1.71	0.0877
11	NCR3LG1	Nerve-Tibial	-5.56	2.62e-08	-3.31	0.000922
11	STARD10	Whole-Blood-DGN	3.87	0.000108	2.6	0.00931
11	TAF1D	Brain-Nucleus-accumbens-basal-ganglia	4.18	2.89e-05	2.77	0.00557
12	KLHL42	Artery-Tibial	-4.76	1.89e-06	NA	NA
12	CTD-2021H9.3	Colon-Transverse	3.88	0.000103	2.25	0.0244
12	CTD-2021H9.3	Muscle-Skeletal	3.7	0.000217	2.21	0.0269
12	TSPAN8	Liver	3.81	0.000137	1.85	0.0643
12	C12orf43	Brain-Anterior-cingulate-cortex-BA24	3.96	7.64e-05	NA	NA
12	CABP1	Adipose-Subcutaneous	4.01	6.13e-05	0.0533	0.957
12	P2RX4	Pancreas	4.23	2.33e-05	1.53	0.127
12	C12orf65	Esophagus-Muscularis	4.27	1.94e-05	0.62	0.536
12	C12orf65	Nerve-Tibial	4.81	1.49e-06	NA	NA
12	CCDC92	Breast-Mammary-Tissue	-4.52	6.14e-06	-0.456	0.648

Table S10 (Continued). Summary table of tissue-level gene associations at regions spanning T2D-associated loci.

Chr	Gene	Model	DIAGRAM Z-score	DIAGRAM p-value	GERA Z-score	GERA p-value
12	CDK2AP1	Nerve-Tibial	3.93	8.37e-05	NA	NA
12	MPHOSPH9	Artery-Tibial	-4.03	5.64e-05	NA	NA
15	C2CD4A	Nerve-Tibial	-3.78	0.00016	-0.533	0.594
15	HMG20A	Muscle-Skeletal	4.04	5.36e-05	2.61	0.00915
15	HMG20A	Pituitary	5.47	4.48e-08	3.41	0.000645
15	HMG20A	Vagina	-4.1	4.07e-05	-0.807	0.419
15	LINGO1	Brain-Putamen-basal-ganglia	3.86	0.000112	2.27	0.0233
15	RCN2	Colon-Transverse	4.63	3.73e-06	3.06	0.00221
15	FAH	Brain-Cerebellum	4.15	3.29e-05	-1.17	0.243
15	ZFAND6	Brain-Cerebellar-Hemisphere	4.53	6.02e-06	-1.67	0.0958
15	ZFAND6	Brain-Cortex	-4.1	4.07e-05	1.3	0.193
15	AP3S2	Adipose-Subcutaneous	4.28	1.83e-05	3.81	0.000142
15	AP3S2	Adipose-Visceral-Omentum	4.11	3.88e-05	3.68	0.000237
15	AP3S2	Adrenal-Gland	4.79	1.69e-06	3.59	0.000328
15	AP3S2	Artery-Aorta	4.32	1.53e-05	3.44	0.000572
15	AP3S2	Artery-Coronary	4.95	7.3e-07	3.75	0.000179
15	AP3S2	Artery-Tibial	4.39	1.13e-05	3.84	0.000122
15	AP3S2	Brain-Anterior-cingulate-cortex-BA24	4.82	1.46e-06	3.64	0.000272
15	AP3S2	Brain-Caudate-basal-ganglia	4.57	4.81e-06	3.72	0.000198
15	AP3S2	Brain-Cortex	4.18	2.88e-05	3.05	0.00231
15	AP3S2	Brain-Frontal-Cortex-BA9	3.97	7.11e-05	2.96	0.00305
15	AP3S2	Brain-Nucleus-accumbens-basal-ganglia	3.97	7.23e-05	2.88	0.00399
15	AP3S2	Brain-Putamen-basal-ganglia	4.43	9.51e-06	3.55	0.000386
15	AP3S2	Breast-Mammary-Tissue	4.25	2.14e-05	3.75	0.000176
15	AP3S2	Cells-EBV-transformed-lymphocytes	4.03	5.6e-05	3.23	0.00122
15	AP3S2	Cells-Transformed-fibroblasts	4.15	3.26e-05	3.49	0.000478
15	AP3S2	Colon-Sigmoid	4.56	5.15e-06	3.84	0.000123
15	AP3S2	Colon-Transverse	4.26	2.01e-05	3.46	0.00054
15	AP3S2	Esophagus-Mucosa	4.56	5.17e-06	3.76	0.000168
15	AP3S2	Esophagus-Muscularis	3.94	8.04e-05	3.5	0.000474
15	AP3S2	Heart-Left-Ventricle	5.03	4.79e-07	3.89	9.82e-05
15	AP3S2	Liver	4.33	1.46e-05	3.62	0.000298
15	AP3S2	Nerve-Tibial	4.69	2.69e-06	3.74	0.000186
15	AP3S2	Ovary	4.69	2.78e-06	3.5	0.000461
15	AP3S2	Pancreas	4.46	8.08e-06	3.6	0.000322
15	AP3S2	Prostate	4.13	3.62e-05	3.13	0.00177
15	AP3S2	Skin-Sun-Exposed-Lower-leg	4.83	1.38e-06	3.7	0.000219
15	AP3S2	Small-Intestine-Terminal-Ileum	5.21	1.88e-07	3.5	0.000464
15	AP3S2	Stomach	4.87	1.11e-06	3.5	0.000471
15	AP3S2	Thyroid	4.78	1.74e-06	3.68	0.000231

Table S10 (Continued). Summary table of tissue-level gene associations at regions spanning T2D-associated loci.

Chr	Gene	Model	DIAGRAM Z-score	DIAGRAM p-value	GERA Z-score	GERA p-value
15	AP3S2	Uterus	4.81	1.53e-06	3.57	0.000353
15	PRC1	Pancreas	-4.67	3.06e-06	-2.9	0.0037
15	PRC1	Whole-Blood-DGN	-4.39	1.15e-05	-2.13	0.0332
15	RCCD1	Adipose-Subcutaneous	5.03	4.84e-07	3.12	0.00181
15	RCCD1	Adipose-Visceral-Omentum	4.65	3.26e-06	2.47	0.0134
15	RCCD1	Artery-Aorta	5.42	5.96e-08	3.06	0.00225
15	RCCD1	Artery-Coronary	4.63	3.67e-06	2.43	0.0149
15	RCCD1	Artery-Tibial	5.25	1.51e-07	3.36	0.000773
15	RCCD1	Brain-Anterior-cingulate-cortex-BA24	5	5.71e-07	3.11	0.0019
15	RCCD1	Brain-Caudate-basal-ganglia	4.77	1.85e-06	2.46	0.014
15	RCCD1	Brain-Cerebellar-Hemisphere	4.81	1.5e-06	2.95	0.00322
15	RCCD1	Brain-Cerebellum	5	5.83e-07	3.4	0.000686
15	RCCD1	Brain-Cortex	5.67	1.4e-08	3.12	0.00178
15	RCCD1	Brain-Frontal-Cortex-BA9	5.67	1.46e-08	2.95	0.00313
15	RCCD1	Brain-Nucleus-accumbens-basal-ganglia	4.01	6e-05	2.69	0.00706
15	RCCD1	Breast-Mammary-Tissue	5.24	1.63e-07	2.65	0.00795
15	RCCD1	Cells-Transformed-fibroblasts	4.41	1.03e-05	1.94	0.0521
15	RCCD1	Colon-Sigmoid	5.46	4.86e-08	2.59	0.00972
15	RCCD1	Colon-Transverse	5.46	4.88e-08	3.21	0.00134
15	RCCD1	Esophagus-Gastroesophageal-Junction	5.45	5.08e-08	2.44	0.0146
15	RCCD1	Esophagus-Mucosa	5.04	4.62e-07	3.09	0.00199
15	RCCD1	Esophagus-Muscularis	4.02	5.71e-05	2.45	0.0144
15	RCCD1	Heart-Left-Ventricle	4.77	1.87e-06	2.11	0.0352
15	RCCD1	Muscle-Skeletal	4.59	4.4e-06	2.72	0.00655
15	RCCD1	Nerve-Tibial	5.54	2.99e-08	3.19	0.00143
15	RCCD1	Skin-Not-Sun-Exposed-Suprapubic	5.22	1.78e-07	3.01	0.00265
15	RCCD1	Skin-Sun-Exposed-Lower-leg	5.19	2.15e-07	3.11	0.00186
15	RCCD1	Stomach	5.68	1.38e-08	3.24	0.00121
15	RCCD1	Testis	5.19	2.09e-07	3.18	0.00149
15	RCCD1	Thyroid	4.98	6.34e-07	3	0.00267
15	RCCD1	Whole-Blood-DGN	4.77	1.87e-06	2.99	0.00282
15	UNC45A	Muscle-Skeletal	3.93	8.38e-05	0.011	0.991
15	VPS33B	Pituitary	5.02	5.09e-07	1.77	0.0767
15	VPS33B	Testis	-4.88	1.06e-06	-2.27	0.023
15	VPS33B	Whole-Blood	-4.43	9.26e-06	-1.03	0.302
15	VPS33B	Whole-Blood-DGN	-4.25	2.11e-05	-1.49	0.137

Table S10 (Continued). Summary table of tissue-level gene associations at regions spanning T2D-associated loci.

Tissue	Mean Square Z-score Rank	Sample Size Rank	Sample Size	Mean Square Z-score
Whole-Blood-DGN	1	1	922	1.17
Adipose-Subcutaneous	2	5	298	1.152
Muscle-Skeletal	3	2	361	1.147
Nerve-Tibial	4	10	256	1.14
Artery-Tibial	5	6	285	1.138
Cells-Transformed-fibroblasts	6	9	272	1.136
Skin-Sun-Exposed-Lower-leg	7	4	302	1.133
Whole-Blood	8	3	338	1.129
Breast-Mammary-Tissue	9	17	183	1.117
Pancreas	10	22	149	1.109
Lung	11	7	278	1.108
Thyroid	12	8	278	1.104
Liver	13	30	97	1.1
Artery-Aorta	14	13	197	1.099
Esophagus-Muscularis	15	12	218	1.095
Adrenal-Gland	16	24	126	1.081
Adipose-Visceral-Omentum	17	16	185	1.079
Esophagus-Mucosa	18	11	241	1.078
Skin-Not-Sun-Exposed-Suprapubic	19	14	196	1.071
Colon-Transverse	20	19	169	1.068
Testis	21	21	157	1.067
Heart-Atrial-Appendage	22	20	159	1.066
Stomach	23	18	170	1.063
Heart-Left-Ventricle	24	15	190	1.062
Brain-Cortex	25	31	96	1.061
Cells-EBV-transformed-lymphocytes	26	27	114	1.057
Esophagus-Gastroesophageal-Junction	27	23	127	1.044
Vagina	28	42	79	1.041
Brain-Nucleus-accumbens-basal-ganglia	29	32	93	1.034
Spleen	30	35	89	1.032
Ovary	31	38	85	1.029
Colon-Sigmoid	32	25	124	1.026
Brain-Cerebellum	33	28	103	1.02
Artery-Coronary	34	26	118	1.018
Brain-Putamen-basal-ganglia	35	39	82	1.003
Brain-Cerebellar-Hemisphere	36	34	89	1.001
Uterus	37	45	70	1
Small-Intestine-Terminal-Ileum	38	43	77	0.9984
Brain-Caudate-basal-ganglia	39	29	100	0.9933
Pituitary	40	36	87	0.9859
Brain-Frontal-Cortex-BA9	41	33	92	0.9843
Brain-Hypothalamus	42	41	81	0.968
Brain-Hippocampus	43	40	81	0.9582
Brain-Anterior-cingulate-cortex-BA24	44	44	72	0.9534
Prostate	45	37	87	0.9217

Table S11. Tissue models ranked by mean square Z-score from predicted gene associations in the trans-ethnic analysis. Shading indicates enriched tissue models based on mean square Z-score rank being less than sample size rank.

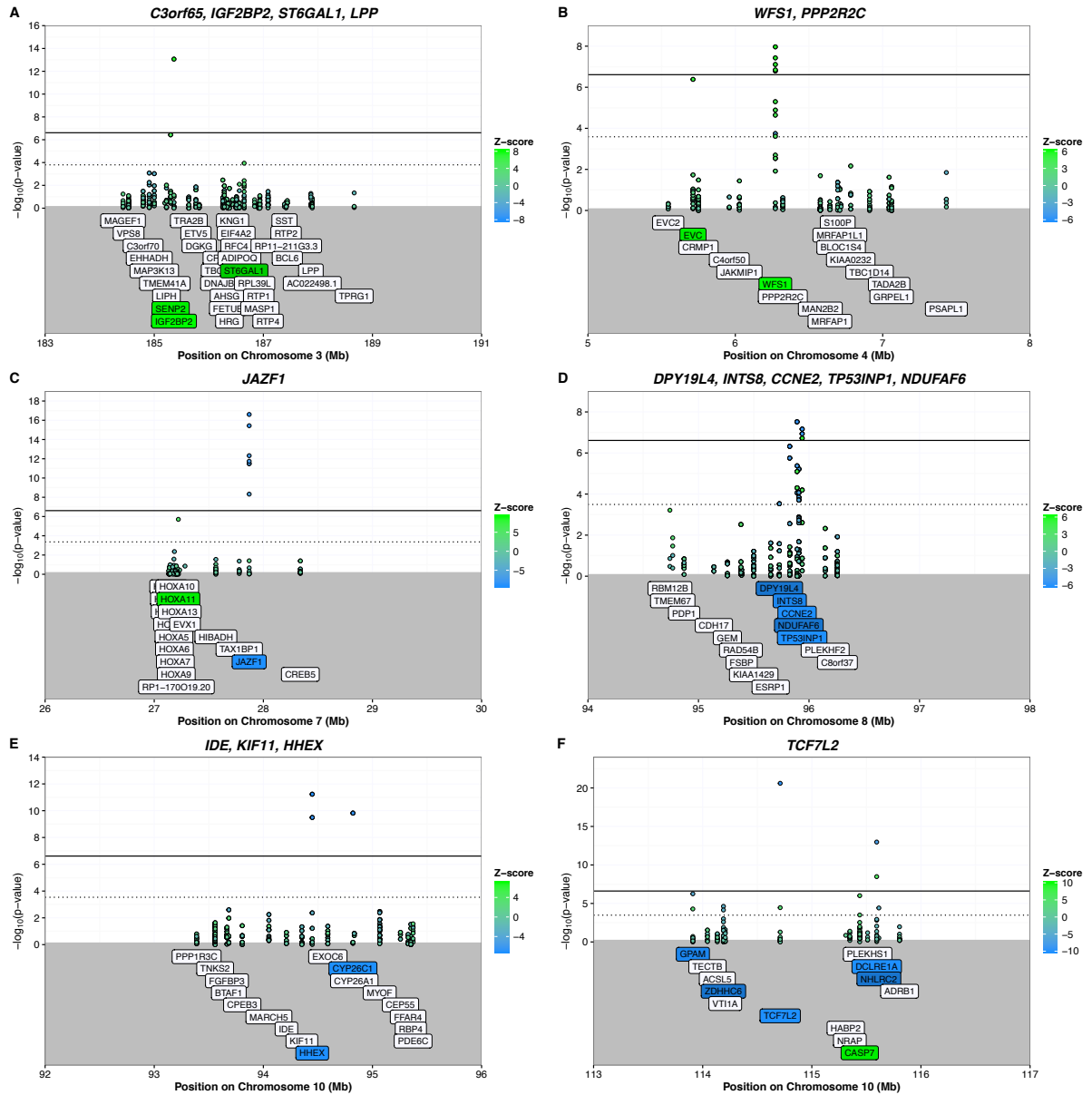


Figure S1. MetaXcan profiles at regions with at least one *reported* gene meeting cross-tissue Bonferroni significance. Solid and dotted lines denote Bonferroni (cross-tissue) and locus-level significance thresholds, respectively. Green and blue fill indicate positive and negative direction of associations (i.e. sign of Z-score), respectively. Label shading shows direction for the top tissue-level association for each meeting MetaXcan significance thresholds.

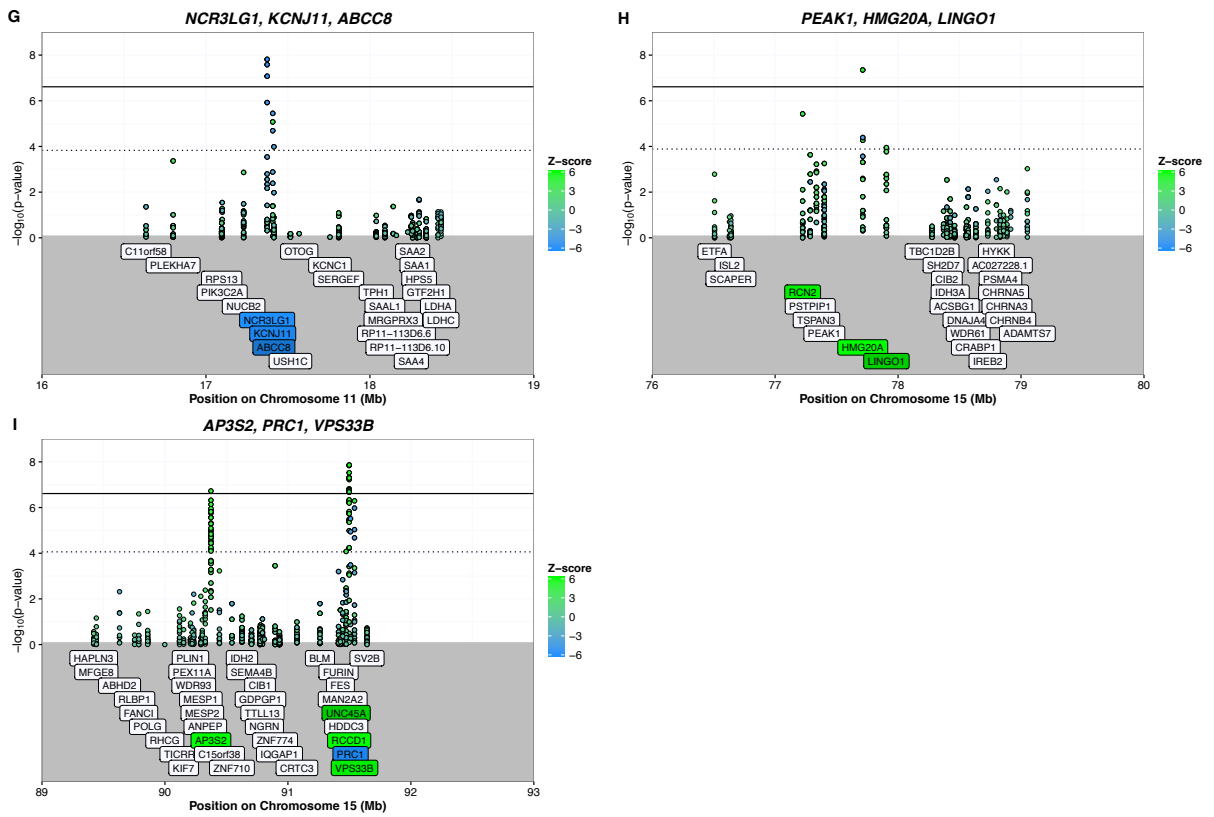


Figure S1 (Continued). MetaXcan profiles at T2D-associated loci

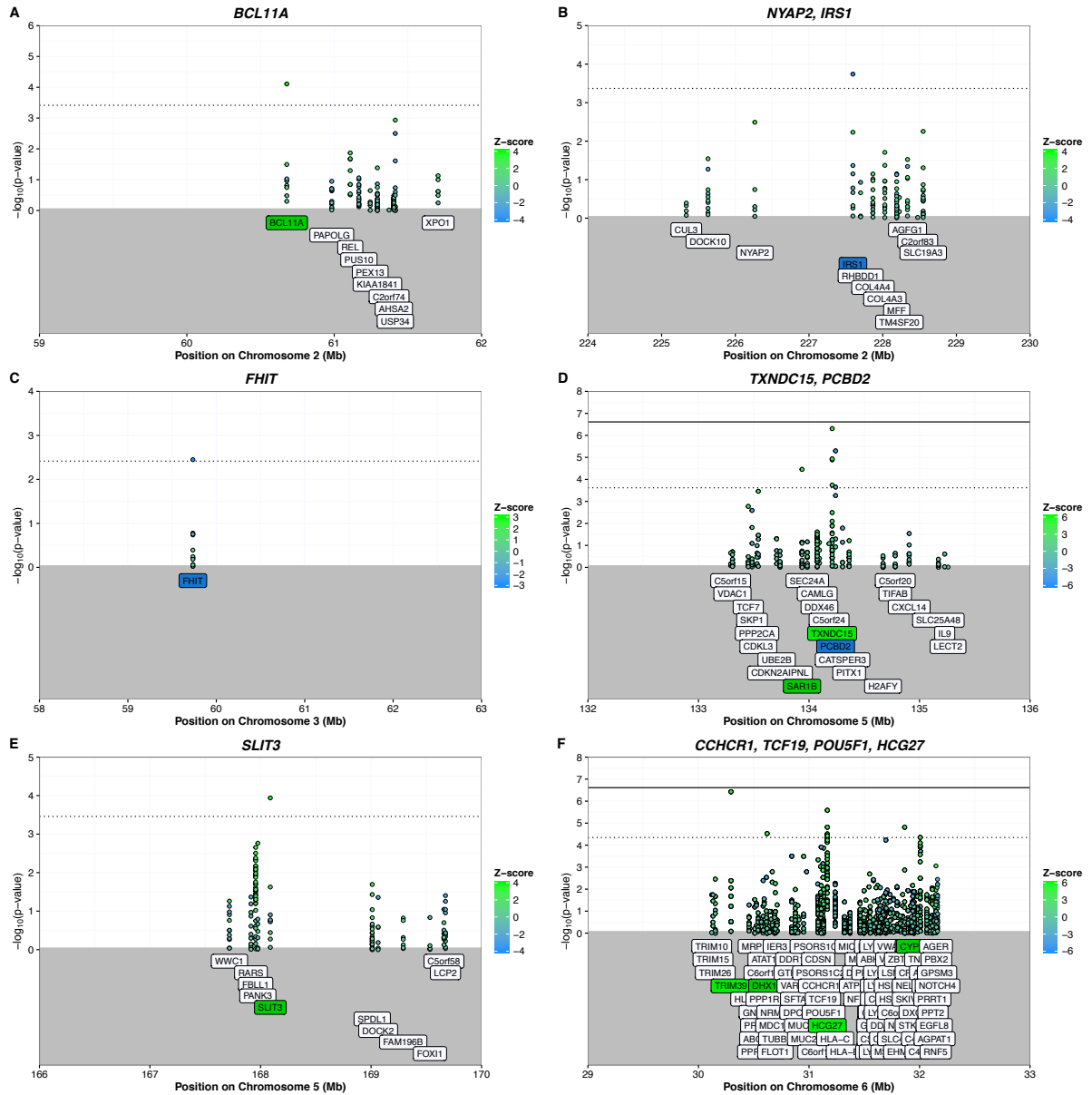


Figure S2. MetaXcan profiles at regions with at least one reported gene meeting locus-level significance. Solid and dotted lines denote Bonferroni (cross-tissue) and locus-level significance thresholds, respectively. Green and blue fill indicate positive and negative direction of associations (i.e. sign of Z-score), respectively. Label shading shows direction for the top x association for each meeting MetaXcan significance thresholds.

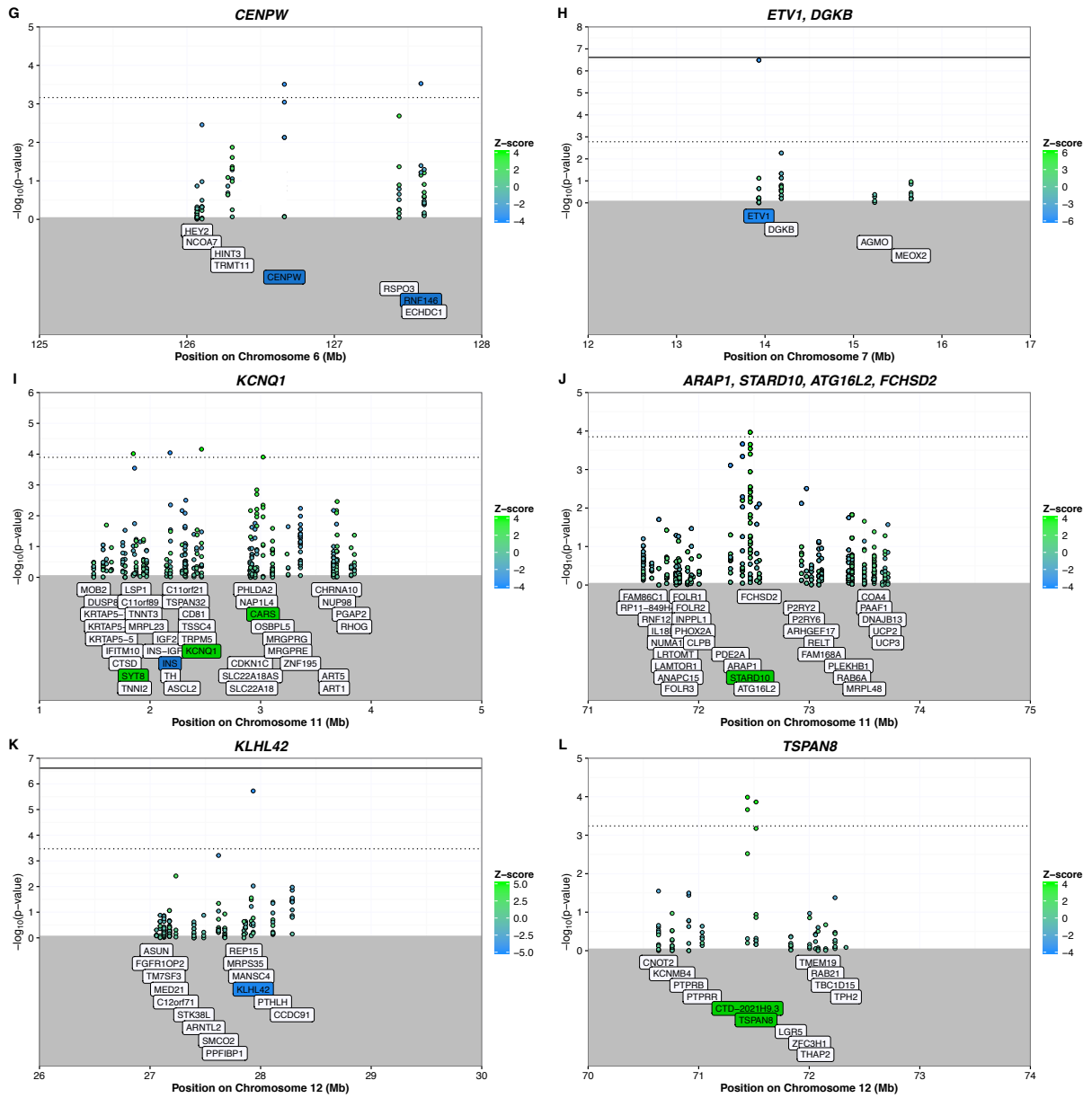


Figure S2 (Continued). MetaXcan profiles at T2D-associated loci

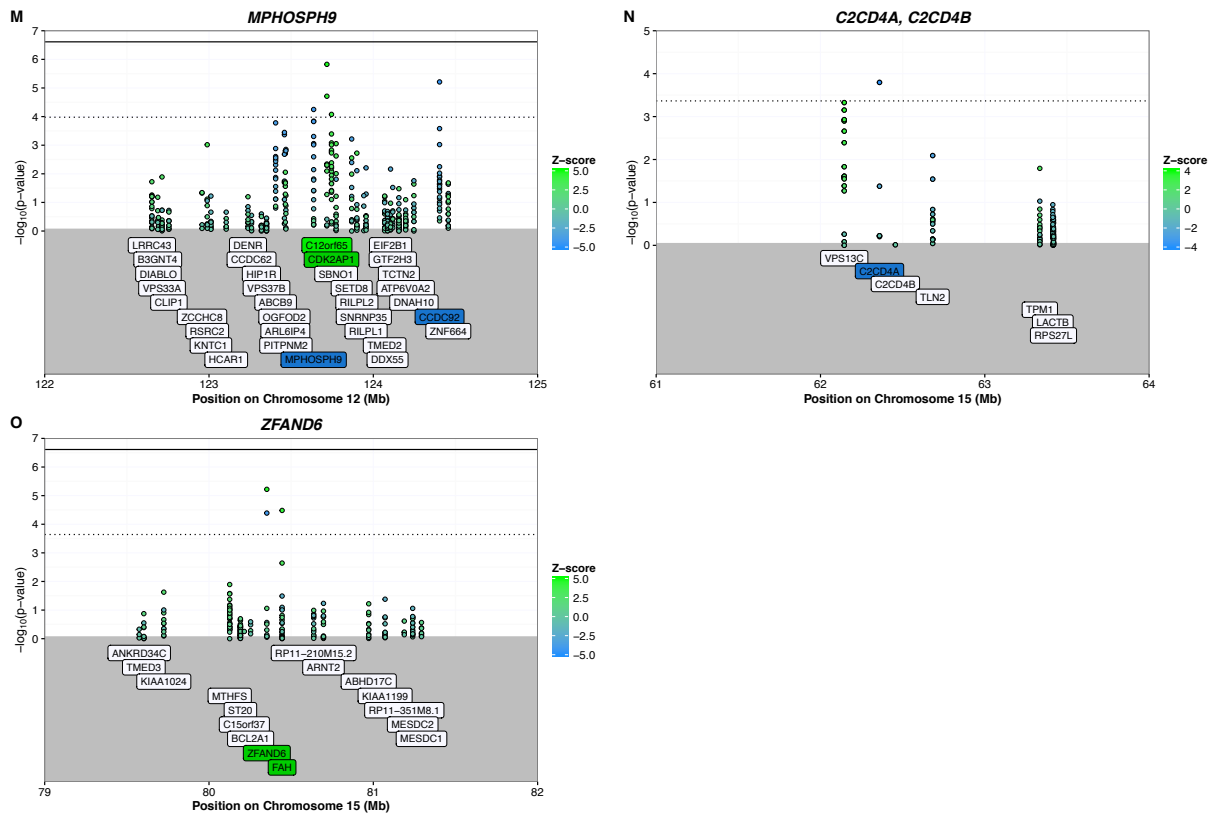


Figure S2 (Continued). MetaXcan profiles at T2D-associated loci

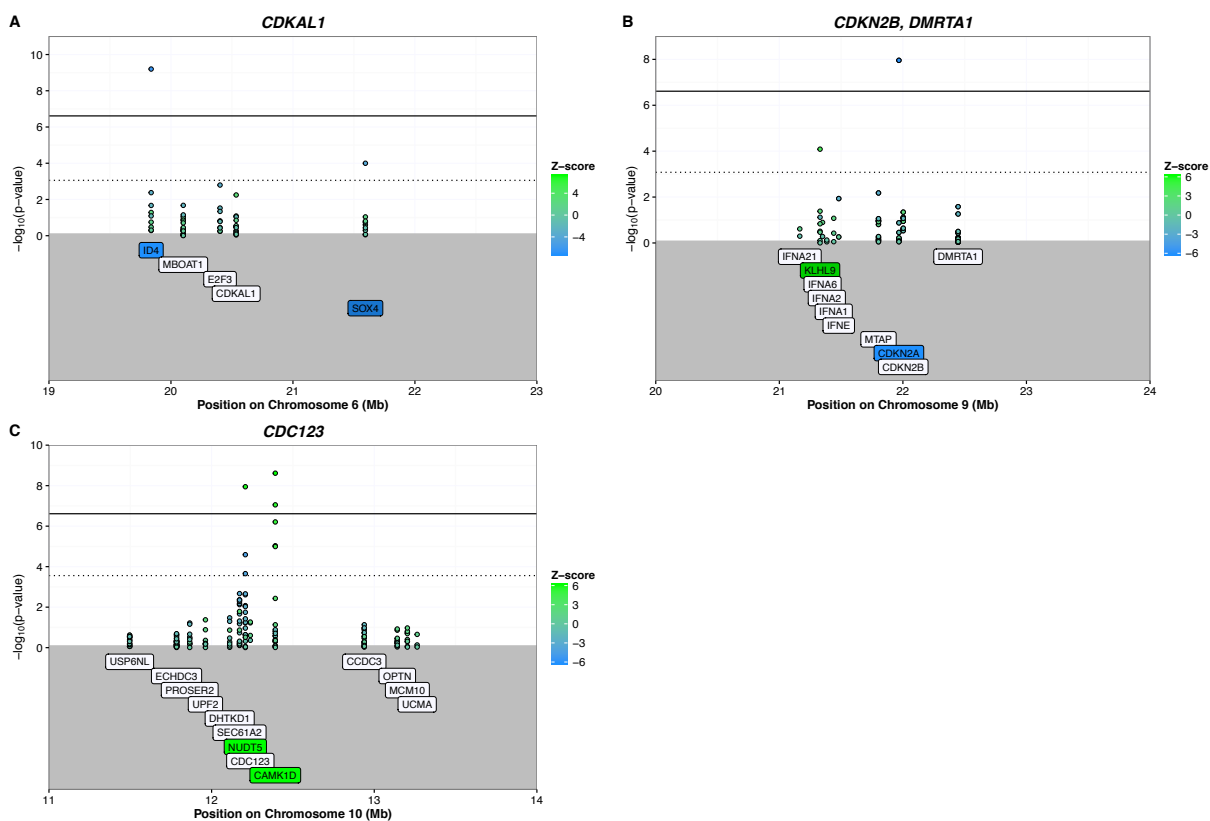


Figure S3. MetaXcan profiles at regions with at least one *novel* gene meeting cross-tissue Bonferroni significance and no significant associations for *reported* T2D genes. Solid and dotted lines denote Bonferroni (cross-tissue) and locus-level significance thresholds, respectively. Green and blue fill indicate positive and negative direction of associations (i.e. sign of Z-score), respectively. Label shading shows direction for the top tissue-level association for each meeting MetaXcan significance thresholds. Note that *CAMK1D* does not map to within 1 Mb of T2D-associated SNPs ($p < 5 \times 10^{-6}$) in the trans-ethnic study and is therefore not considered a *reported* gene in this study although it is reported elsewhere.

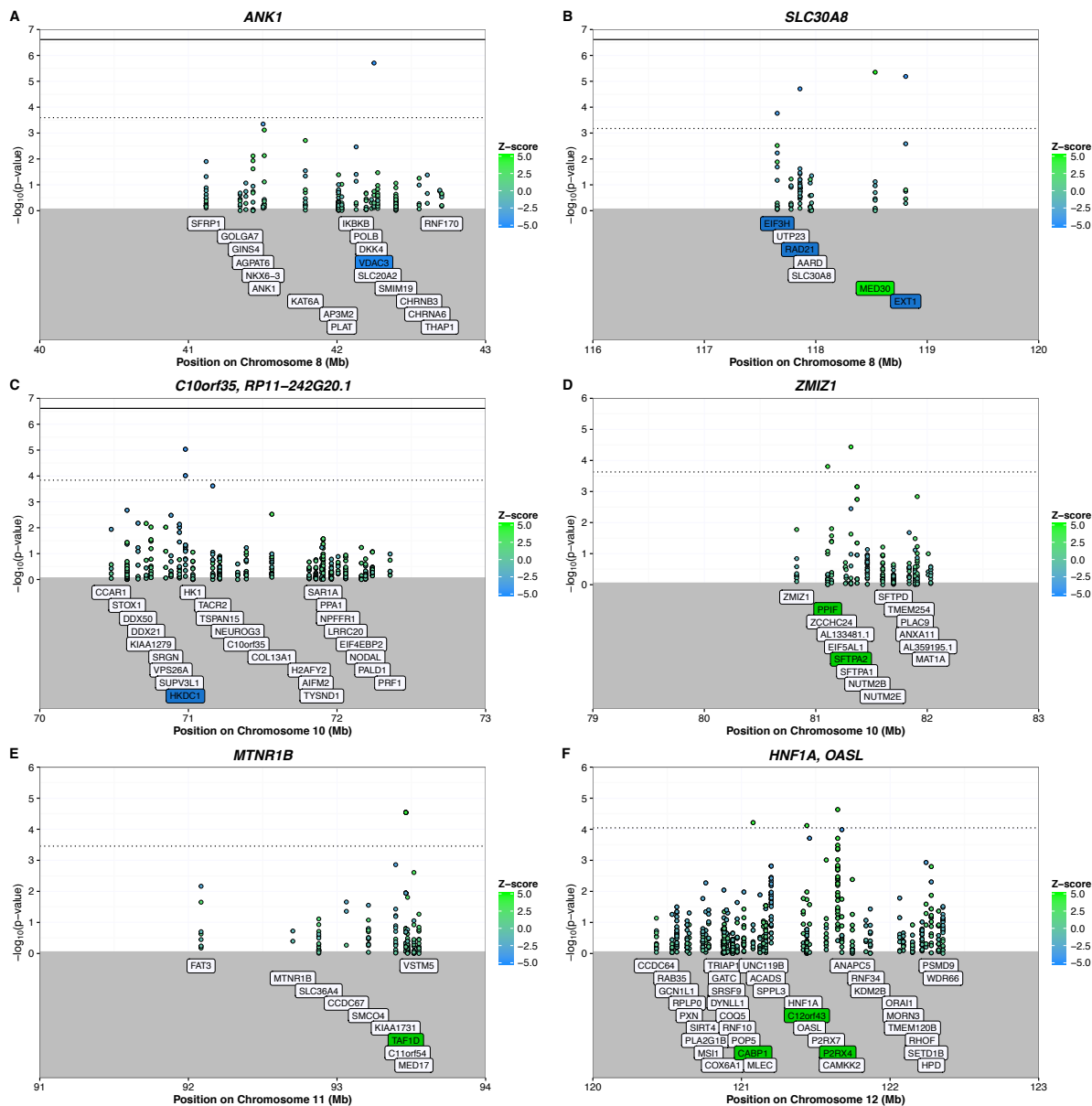


Figure S4. MetaXcan profiles at regions with at least one *novel* gene meeting locus-level significance and no significant associations for *reported* T2D genes. Solid and dotted lines denote Bonferroni (cross-tissue) and locus-level significance thresholds, respectively. Green and blue fill indicate positive and negative direction of associations (i.e. sign of Z-score), respectively. Label shading shows direction for the top tissue-level association for each meeting MetaXcan significance thresholds.